



CONCEPTS *of* CHEMICAL DEPENDENCY

10th edition

HAROLD E. DOWEIKO



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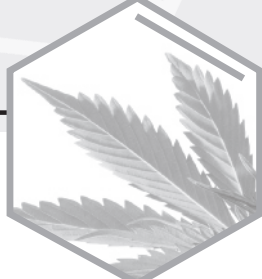
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CONCEPTS *of* CHEMICAL DEPENDENCY

10th edition

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In loving memory of Harold Doweiko.

For Jan.

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Preface

The world of the neurosciences is constantly changing. New discoveries about the process of neurotransmission, how neurotransmitter receptor sites are distributed throughout the brain, how certain chemicals force or block the action of various regions of the brain, how they damage neurons or aid in their recovery, how the brain interacts with the body to form the concept of a unified “self,” all conspire to make a textbook such as this exceptionally difficult to keep current. Many long-cherished theories have been discarded, while new information leads to the formation of new theories, or suggests new directions for theoretical inquiry. An excellent example is Koob’s (2009) assertion that scientists are only now starting to explore the role of glial cells in the brain. For example, the glial cells make up 90% of the brain’s mass but were until recently overlooked by neuroscientists, who dismissed these cells as simply providing metabolic support for the neurons. It is now understood that while glial cells do indeed carry out this function, they also play a role in the process of neurogenesis and, as was recently discovered, are involved in a form of neurotransmission that both parallels and is independent of the neuron neural networks in the brain.

Over the years, there have been a number of changes made to this text, and this process has continued with the current edition. New research is cited, and the process of publishing journal articles online before the publication of the printed version has resulted in the citation of numerous journal articles that were “published on-line prior to print.” Further, since research suggests that substance use patterns might differ between young adults who go on to attend college and those who do not, a new chapter that focuses just on substance use issues in the college student population has been added to the text. Information about the synthetic THC-like compounds that became popular drugs of misuse in the first months of this decade have also been reviewed. Several of the chapters have been rewritten in an attempt

to avoid duplication of material. Out of curiosity I tried to count every change made to the manuscript from the addition or deletion of a reference to the addition of new material and deletion of material not thought relevant, movement of a section to another part of a chapter so that it would be more appropriate there, etc., and gave up at 600.

Over the years, several instructors have contacted the author to inquire about the chapter sequence decisions. It is difficult to write a text that will be used across a range of diverse fields of study in the order that will meet the demands of each class (psychology, sociology, nursing, and substance misuse counseling, to name a few of the college classes that have used earlier editions of this text). I do believe that it is important to review the drugs of misuse and their effects first so that the student might understand why the misuse of these compounds is so appealing.

The author of this text was, for example, speaking at a seminar about the total amount of amphetamine that an addict might inject in a “speed run.”¹ when a nurse blurted out that the hypothetical person could not *possibly* be injecting that much methamphetamine because it was dangerous and potentially fatal. “Welcome to the world of amphetamine misuse” was the author’s response. Substance misuse is a different reality than the one taught in nursing schools, psychology programs, sociology programs, or even medical school. On more than one occasion the author of this text has been approached by a trauma surgeon to explain why a person would knowingly expose themselves to doses of anabolic steroids, and how this would affect their behavior. On many occasions, students or seminar participants have expressed surprise at some of the contaminants or adulterants found in illicit drugs. Trying to explain that for the person addicted to

¹Discussed in the chapter on amphetamine misuse and addiction.

these compounds the contaminants are an unwelcome inconvenience but a necessary evil that must be suffered to use the desired drug(s). For these reasons the author of this text has adopted the philosophy that to understand and treat substance use disorders, you need to first understand the chemicals being misused and their effects.

Acknowledgments

It is not possible to thank all of those people who have provided so much support during the preparation of this edition. I would like to thank Dr. David Metzler for his willingness to part company with many copies of various journals over the years. This allowed me access to many of the references cited in this text, and his kindness is appreciated. In addition, I would like to thank in addition, I would like to thank Dr. Amelia Evans for her invaluable contributions to this edition.

DISCLAIMER

The clinical examples used in this text are based on a wide variety of sources, including (but not limited to): characters as portrayed in various movies, books, or television programs, news stories from the media, and clinical examples provided in various references cited at the end of this text or as portrayed by presenters at various workshops that the author has attended. *All examples provided are hypothetical in nature. Any resemblance to any person, living or dead, is entirely due to chance and should not be inferred by the reader.* Further, the practice of substance misuse counseling or psychotherapy is very complex and the practitioner should be familiar with a wide range of resources in conducting their practice. *Neither the author nor the publisher shall be liable or responsible for any harm, loss, or damage allegedly arising from any information or suggestion made in or omitted from this text.*

Why Worry About Substance Misuse or Substance Use Disorders?

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 1.1 Understand why substance misuse and SUDs are legitimate problems for society
- 1.2 Identify the scope of the problem of alcohol and drug misuse and SUDs
- 1.3 Understand the costs related to alcohol and drug misuse and SUDs
- 1.4 Describe those who encounter and treat individuals with SUDs
- 1.5 Comprehend the lack of education prevalent in those who encounter individuals with SUDs

Doctors are men who prescribe medications of which they know little, to treat diseases of which they know less, in human beings of whom they know nothing.

—Voltaire quotes (2015)

Introduction

It is indeed unfortunate that the above quotation from Voltaire could easily be applied to the study of the substance use disorders (SUDs). Some researchers speak with great authority about persons with a SUDs, demonstrate increased or decreased activity in the brain as measured by one parameter or another when under the influence of chemicals, or show that certain genes are activated or deactivated in critical phases of development significantly more often in those persons with a SUDs than in the general population, as if these things *caused* the chemical use problem. Such things might reflect contributing factors but might equally be the end result of the SUDs itself. However, the most important point is the SUDs involves not nameless statistics in journal or newspaper articles, but *people*. Whether directly or indirectly, SUDs affect each of us (Hari, 2015).

People with SUDs are often ostracized by people in “polite” society who either focus on the substance as if it were the problem or look down on those who have become addicted as if they were a lower life form (Maté, 2010). Researchers now believe that collectively SUDs (SUDs) affect 1 in every 11 Americans over the age of 11 years and cause more than 60,000 deaths a

year¹ in this country alone (Frakt & Bagley, 2015). SUDs² might take any number of forms, including the subset of SUDs known as alcohol use disorders (AUDs) and nicotine use disorders (NUDs). Individuals who misuse prescription drugs fall under the rubric of having an SUD, but often are able to successfully hide their prescription drug use from others because their drugs were *prescribed* by a health care professional. A subgroup of individuals who misuse substances indulge in infrequent use of illegal drugs such as the hallucinogens, cocaine, illicit narcotics, and marijuana.³ Finally, there are those individuals who misuse compounds not normally intended for human use such as inhalants or anabolic steroids.^{4,5}

The face of SUDs evolves over time: One compound or another gains widespread acceptance and then is replaced by the next popular drug. The increasing use of social media allows potential customers to arrange to meet their suppliers at mutually agreed upon locations to carry out their illegal transactions. Alcohol and nicotine (and in some states marijuana) hold a unique position in this process: Their use is legal for persons over a certain age, and the level of alcohol or tobacco use has remained relatively constant in spite of widespread knowledge of the physical, social, and financial toll that the use of these compounds causes. Additionally, marijuana continues to gain acceptance in many states, not only for medicinal use, but for personal recreational use as well. There have been

initiatives to ban the use of these compounds over the years, with arguable success, an excellent example being the Prohibition era in the United States. Although alcohol and tobacco are legal, they do share one characteristic with the other drugs that are misused: They exact a terrible cost on the individual and society. In this chapter, we will begin to examine the impact of SUDs on society and the individuals who make up that society.

SUDs as Unsuspected Influences on Society

It is difficult to identify every way in which SUDs influence society. It has been estimated that the direct and indirect costs of SUDs consume *over 15%* of the average state's budget⁶ (National Center on Addiction and Substance Abuse at Columbia University [CASA], 2009a). Each year in the United States individuals who misuse illicit drugs spend \$100 billion to purchase those drugs (Kilmer et al., 2014b), while another \$467 billion is spent annually on substance misuse and addiction (CASA, 2015). This is misleading, however, since politicians slide part of the expense from one budgetary column to the next (CASA, 2009a), and only 2% of the money spent goes toward prevention and treatment (CASA, 2015). The cost of incarcerating those who are convicted of drug-related offenses is not considered part of the cost of the "war on drugs" but a part of the Department of Corrections budget. The cost of providing health care for the families of those convicted of drug-related offenses becomes part of the Department of Human Services budget, and so on (Cafferty, 2009).

In the 21st century, the rising cost of health care in the United States has become hotly debated. Politicians speak at length about the rising cost of health care, but ignore the impact of SUDs, as evidenced by the following facts:

- Approximately 20–25% of patients seen by primary care physicians have a SUDs (Jones, Knutson & Haines, 2004; McLellan et al., 2017).

⁶Alcohol-related disease results in approximately 20,700 deaths each year in this country, a figure that does not include persons who die in alcohol-related accidents or who are killed in an alcohol-related homicide (Johnson, 2010).

¹This number excludes those persons who lose their lives to tobacco- or alcohol-related illness.

²Because the term *alcoholic* has been found to actually deter many in need of treatment for their alcohol use problem from seeking rehabilitation (Keyes et al., 2010), the term "alcohol use disorder" will be used to indicate persons who misuse or are addicted to alcohol, while the more inclusive term "SUDs" is used to address the entire spectrum of drug use disorders.

³The legal status of marijuana is highly variable at this time because some states are allowing its use for medical disorders while other states have legalized possession in small quantities for personal use.

⁴While many of the steroid compounds being misused were indeed intended for human use, they are used at dosage levels far in excess of what is medically acceptable, and thus could be said not to be intended for human use. Further, many of the steroid compounds being misused were not intended for use by humans, but were designed for use with animals and diverted to the illicit market or manufactured in illicit laboratories.

⁵Membership in these subgroups is not fixed or mutually exclusive. A person might belong to more than one subgroup simultaneously or move from one subgroup to another over time.

- Substance misuse and SUDs can cause or exacerbate more than 70 health conditions (CASA, 2015).
- Excessive alcohol use was a factor in 50% of all deaths from acute traumatic injuries (Baron, Garbely, & Boyd, 2009).
- Approximately one million hospital emergency room visits are the result of illicit drug use (Centers for Disease Control and Prevention, 2010b).
- Approximately 40% of *all* hospital admissions can be tied either directly or indirectly to alcohol use/misuse (Baron et al., 2009; Greenfield, 2007; Greenfield & Hennessy, 2008).
- Hospitalized persons with a SUDs are more likely to require rehospitalization within 30 days of discharge than nonusers (Walley et al., 2012).
- Approximately 25% of those individuals on Medicaid have a SUDs. As this group ages, the cost of their medical care increases at a higher rate than for age-matched individuals without an SUD ("Substance abuse adds millions," 2008).
- There were 47,055 drug overdose deaths in 2014, of which 28,047 involved a narcotic either alone or in combination with other chemicals (Rudd, Aleshire, Zibbell, & Gladden, 2015).

SUDs are frequently intertwined with psychiatric problems, further contributing to the rising cost of health care as evidenced by the facts that:

- The SUDs are a factor in 50–75% of all psychiatric hospital admissions (Miller, 2004).
- Of hospital stays that are non-pregnancy/delivery related, 17% involve individuals with psychiatric disorders co-occurring with SUDs (Heslin, Elixhauser, & Steiner, 2015).
- One-third of those persons who commit suicide have an alcohol use disorder (Karch, Dahlberg, & Patel, 2010).
- Between 40 and 60% of those individuals who committed suicide were intoxicated at the time of their deaths,⁷ and 10% had evidence of other drugs in their bodies at the time of their death (Karch, Cosby, & Simon, 2006; Scott & Marcotte, 2010).
- Traumatic brain injury (TBI) accounts for almost one-third of trauma-related deaths in the United

States each year, and between 29 and 52% of those who survive the TBI have alcohol in their bodies at the time of admission to a hospital (Miller & Adams, 2006).

- Neurological damage that is apparently induced by long-term heroin abuse appears to continue for at least three years after the individual discontinues the abuse of the substance⁸ (Zou et al., 2015).

SUDs and interpersonal violence: There is a well-documented relationship between SUDs and violent behavior that has remained relatively constant over the years. Yet ongoing research is needed to fully understand the impact of SUDs and violence (United Nations, 2016). Half of all perpetrators of a violent crime have been found to have been drinking before the commission of that crime (Coghlan, 2008; Parrott & Giancola, 2006). Researchers have found that adults misusing substances are 2.7 times as likely to have been physically abused as a child and 4.2 times as likely to have neglected a child than were peers who do not misuse substances (Ireland, 2001). Alcohol is involved in 40–86% of all homicides committed in the United States (Parrott & Giancola, 2006)⁹ and 40% of homicide cases in Europe (Coghlan, 2008). Illicit drug use increases a woman's chance of being murdered by her significant other by as much as 28-fold, even if she was not misusing chemicals herself at the time of her death (Parrott & Giancola, 2006). Forty percent of homicide victims across 17 states were found to have alcohol in their systems (Naimi et al., 2016).

The Scope of the Problem of the SUDs

At least half of the world's population has used at least one psychoactive substance at least once, with alcohol being the most commonly used psychoactive chemical (Leamon, Wright, & Myrick, 2008). However, when alcohol use is not included in the assessment of the scope of SUDs, close to 250 million people, or just above 3% of the entire population of the world between 15 and 64, used an *illicit* substance in 2014 (United Nations, 2016). The majority of those who use a psychoactive substance do so on a short-term experimental

⁷The discrepancy between these two figures is explained by the fact that many of those who commit suicide consume alcohol as a way to steel their courage before taking their lives, while others commit suicide impulsively while intoxicated.

⁸It is not known whether this is a direct result of the heroin use, exposure to any of the "fillers" or contaminants in the heroin, or polydrug use, but the results strongly suggest heroin as the primary cause for the neurological damage.

⁹These different estimates reflect the different methodologies used in different research studies.

basis and rarely present the problems to society seen in cases of substance *addiction*. The team of Grant and colleagues (2015) utilized *DSM-5* criteria and concluded that approximately 10% of the population will meet the criteria for physical addiction at some point in their lives and that 4% do so any given point in time. The majority of those individuals who are actively addicted to chemicals fail to receive any form of treatment, according to the authors.

A thriving black market,¹⁰ which is further aided by the availability of drugs via internet sources including the dark net, has evolved around the world to meet the demand for illicit drugs¹¹ created by those misusing substances or by those who are addicted to one or more chemicals. In spite of strict legal sanctions, this distribution system is quite resilient. The worldwide illicit drug trade has been previously estimated to be a \$800 billion/year industry, making it larger than the annual gross domestic product of 90% of the world's countries ("Vital signs," 2007; United Nations, 2012).

In a sense, drug use might be said to be an "American way of life." Close to 30 million people in the United States over age 12 smoked cigarettes daily, 15.1 million had an alcohol use disorder, and 7.7% had an illicit drug use disorder in 2016 (Substance Abuse and Mental Health Services Administration [SAMHSA], 2017). Keep in mind that it is possible for an individual to be in two or all three of the categories listed above. Still, with less than 5% of the world's total population, the United States consumed \$100 billion a year of the cocaine, marijuana, methamphetamine, and heroin produced on this planet from 2000 to 2010 (Kilmer et al., 2014a). Each day in the United States, approximately 8,000 people will try an illicit drug for the first time (Lemonick & Park, 2007; SAMHSA, 2009), with over 4% of individuals age 13 and older initiating illicit drug use in 2015 (SAMHSA, 2016). Many of these individuals will probably only experiment with illicit drugs out of curiosity for under 12 months¹² and then discontinue or curtail further use of that compound (Center for Substance Abuse Research, 2008).

The most commonly used drug worldwide is marijuana (United Nations, 2016), with 44% of those age 12 and older in the United States acknowledging marijuana use at some point in their lifetime, with 24 million acknowledging use in the past month (SAMHSA, 2016, 2017). The second figure still means that close to 5 million people over the age of 12 misused an illicit compound other than marijuana in the

month preceding the survey (SAMHSA, 2017). An interesting research study methodology utilized by Banta-Greene and colleagues (2009) tested waste water from both rural and urban areas and found measurable amounts of cocaine and methamphetamine metabolites, underscoring the widespread misuse of these compounds in this country. In the next section, we will more closely examine the scope of the problem of SUDs in this country.

Alcohol Use, Misuse, and Alcohol Use Disorder

As the estimated 176 million people in the United States who ingest alcohol at least once each year can attest, alcohol is a popular recreational chemical (SAMHSA, 2016). For most of these people, alcohol will not become a problem in any sphere of their lives. However, between 8 and 16 million persons in the United States do become physically dependent on alcohol, while another 5.6 million are believed to misuse it on a regular basis (Bankole & Ait-Daoud, 2005). This may underestimate the total number of persons with an alcohol use disorder, since many high-functioning persons with an alcohol use disorder are able to successfully hide the fact from friends, family, and coworkers, possibly for decades (Benton, 2009).

For the average person, alcohol might represent a pleasant diversion from the stress of daily living; however, a minority of those who drink consume a disproportionate amount of the alcohol produced. Ten percent of individuals who drink alcohol consume 60% of the alcohol consumed in the United States, while the top 30% of individuals who drink consume 90% of the alcohol consumed in this country (Kilbourne, 2002). If their drinking has resulted in their suffering social, physical, emotional, or vocational consequences,¹³ then they may have an AUD. The majority of those in the United States who do develop an AUD are predominantly male by a ratio of approximately 2 or 3 to 1 (Kranzler & Ciraulo, 2005a; SAMHSA, 2016). These figures underscore the danger of alcohol use and misuse in spite of its legal status as a socially acceptable recreational compound for adults.

Estimates of the Problem of Opiate Misuse and Opioid Use Disorder¹⁴

When many people in the United States hear the term "narcotics" they usually think of heroin, a drug that does indeed account for 71% of the opiate use disorders around the world

¹⁰See Glossary.

¹¹Or illegal alcohol to minors or in areas where alcohol use is prohibited.

¹²However, it is important to keep in mind that even those who are merely curious about the effects of an illicit drug(s) run the risk of becoming addicted.

¹³The topic of determining whether a person has an AUD will be discussed later in this book.

¹⁴For purposes of this text, the terms *opiod*, *opiate*, and *narcotic* will be used interchangeably, although, as will be discussed in Chapter 11, there are technical differences between these terms.

(United Nations, 2012). Globally, it has been estimated that 17.4 million people use opiates such as heroin and opium (United Nations, 2016). In the United States, current estimates suggest that approximately 5 million people have used heroin at some point in their lives and that there are over 600,000 with a heroin use disorder (SAMHSA, 2016, 2017).

Unfortunately, heroin is only one of a wide range of opioids that might be obtained and misused.¹⁵ In the United States, there are a growing number of people who are addicted to prescription narcotic analgesics, either prescribed for the user or obtained from illicit sources. An estimated 1.8 million people in this country have a use disorder related to prescription opioids, with 3.3 million misusing prescription opioids (SAMHSA, 2017). The problem of medication diversion is an ongoing one in the United States, with the result that many individuals addicted to opiates support their opioid misuse almost exclusively on prescribed medications obtained either from a physician or from illicit sources. Thus, the estimates above *underestimate* the total number of people addicted to an opiate in this country by an unknown margin.

Estimates of the Problem of Stimulant Misuse and Stimulant Use Disorder¹⁶

Globally, the problem of central nervous system (CNS) stimulant misuse¹⁷ includes the 35.7 million people around the world misusing a CNS stimulant at least once each year (United Nations, 2016). About 1.7 million people in the United States use methamphetamine compounds at least once each year (SAMHSA, 2016). Much of the methamphetamine enters from other countries, although there are still local “labs” making small amounts of methamphetamine for local consumption (United Nations, 2016). The media in this country often focuses on local CNS stimulant use disorders; however, in reality, only 15% of those who misuse CNS stimulants live in North America (United Nations, 2012). As it is true for narcotic analgesics, an unknown percentage of prescribed CNS stimulants is diverted to the illicit market, providing a pool of unrecognized individuals who rely on these stimulants.

Estimates of the Problem of Cocaine Misuse and Cocaine Use Disorder

The number of individuals who use or are addicted to cocaine in the United States has actually gone down in recent years

(United Nations, 2016). Globally, approximately 18.3 million people use or are addicted to cocaine (United Nations, 2016). In this country, it has been estimated that there are close to 2 million people who use cocaine monthly, and close to 40 million people who have used it at some point in their lives (SAMHSA, 2016, 2017). The true scope of cocaine misuse/addiction in the United States is confused by the fact that, in spite of its reputation, researchers during the last wave of cocaine use concluded that only 3–20% of those who used cocaine would go on to become addicted to it¹⁸ (Musto, 1991).

Estimates of the Problem of Marijuana Use, Misuse, and Cannabis Use Disorder

Globally, it is estimated that at least 182.5 million people have used marijuana in the past 12 months (United Nations, 2016). An estimated 24 million people are thought to be current users of marijuana in the United States (SAMHSA, 2017). Approximately 44% of the entire population of this country is thought to have used marijuana at least once, and, 8.9% have used marijuana in the past month (SAMHSA, 2016, 2017).¹⁹

Estimates of the Problem of Hallucinogen Misuse²⁰

Many researchers question whether it is possible to become *addicted* to hallucinogens. But it is thought that perhaps 15% of the population of the United States has used a hallucinogen at least once in their lives (SAMHSA, 2016). It is estimated that 1.4 million persons in this country have used a hallucinogenic compound in the past month (SAMHSA, 2017).

Estimates of the Problem of Tobacco Use and Tobacco Use Disorder

Tobacco is a special product: It can be legally purchased by adults, yet it is acknowledged to be destructive and addictive.

¹⁸The danger, as will be discussed again in Chapter 9, is that it is impossible to predict at this time *which* individual will go on to become addicted to cocaine, and thus the use of this compound is discouraged, if only for this reason. Other dangers associated with cocaine use/addiction will be discussed in Chapter 9.

¹⁹Although most people do not think of marijuana as a potentially addictive substance, as will be discussed in Chapter 10, some individuals do indeed become addicted to it.

²⁰This is a difficult subject to discuss in depth since some researchers classify MDMA as a hallucinogen, others classify it as an amphetamine, and still others call it a hallucinogenic amphetamine compound. In this text it will be classified as a hallucinogen. See Chapter 12 for more details on this issue.

¹⁵The topic of opioid misuse is discussed in Chapter 11.

¹⁶This topic is discussed in more detail in Chapter 8.

¹⁷Which includes the misuse of methylphenidate and the various amphetamines.

Unfortunately, tobacco products are easily available to adolescents, and in some cases to children. More than one billion people in the world smoke tobacco, yet tobacco kills more than 7 million people each year (World Health Organization, 2017). Researchers estimate that approximately 23.5% of the entire population of the United States are current tobacco users, of which number 66.8% smoke only cigarettes (SAMHSA, 2017). An estimated 171 million individuals in this country over age 11 have used tobacco at least once, which accounts for almost 64% of the population (SAMHSA, 2016).

The Cost of Chemical Misuse and SUDs

Globally, drug use disorders are the sixth leading cause of disease in adults (Leamon et al., 2008). Fatal drug overdoses have increased by 137% over a 14-year period in the United States (Rudd et al., 2016). Illicit drug use is thought to cost the global economy \$880 billion a year, with alcohol use disorders costing the world economy another \$880 billion a year (“Vital signs,” 2007). In the United States, alcohol and drug use disorders are thought to drain at least \$375 billion/year from the economy (Falco, 2005). The annual toll from the various diseases associated with illicit drug use in the United States, combined with the number of drug-related infant deaths, suicides, homicides, and motor vehicle accidents, is estimated to be approximately 12,000–17,000 people a year (Donovan, 2005; Miller & Brady, 2004; Mokdad, Marks, Stroup, & Gerberding, 2004).

All the estimates cited in the last paragraph are in addition to the 20 million Americans who have died since 1964 from tobacco-related causes (U.S. Department of Health and Human Services, 2012). Further, approximately 100,000 people die each year in the United States due to chronic or acute alcohol use (Centers for Disease Control and Prevention, 2013). Alcohol use disorders contribute to or exacerbate 70 different disorders (CASA, 2015; Room, Babor, & Rehm, 2005). A person might die from one of the disease states exacerbated by their drinking, but the cause of death recorded on the death certificate will be the disease state itself and not the individual’s alcohol misuse. If one were to include these “indirect” alcohol-related deaths it becomes clear that alcohol either directly or indirectly causes as many deaths each year in the United States as do tobacco products (Room et al., 2005).

The Cost of Alcohol Use/Misuse/AUD

In the United States, alcohol dependence ranks as the third most common cause of preventable death (Johnson, 2010).

The annual economic impact of overuse of alcohol in this country is thought to be at least \$250 billion a year, which is approximately \$2.05 per drink consumed (Sacks, Gonzales, Boucher, Tomedi, & Brewer, 2015). Between 2006 and 2010 in the United States, of those for which information related to alcohol could be obtained, one out of every 10 deaths was related to excessive drinking (Stahre, Roeber, Kanny, Brewer, & Zhang, 2014).

It has been estimated that the complications brought on by alcohol use account for 15–25% of the total annual expenditure for health care each year in the United States (Anton, 2005; Swift, 2005). Although only 5–10% of the population in this country has an AUD, they consume a disproportionate amount of the yearly health care expenditures, as evidenced by the fact that between 15 and 30% of those individuals in nursing homes are thought to be there either as a direct or indirect result of their AUD (Schuckit, 2006a). Alcohol misuse is thought to be a factor in approximately 40% of all motor vehicle accidents (Craig, 2004; Savage, Kirsh, & Passik, 2008), and 40% of those who die as a result of these accidents were not the ones driving (Hingson & Rehm, 2014).

The Cost of Tobacco Use Disorders

Although it is legally produced, purchased, and used by adults without restriction, tobacco use extracts a terrible toll around the globe. Globally, 7 million people a year die as a result of tobacco products, with more than 6 million deaths related directly to the individual’s tobacco use (World Health Organization, 2017). The annual economic losses from in just the United States alone for medical care related to smoking approach \$170 billion/year (Xu, Bishop, Kennedy, Simpson, & Pechacek, 2015). One in every five deaths in this country can be directly traced to smoking-related illness (Sadock, Sadock, & Ruiz, 2015). This figure does not include those persons who die as a result of exposure to “secondhand” or “environmental” tobacco smoke each year in this country.

The Cost of SUDs

It has been estimated that when one totals the cost of premature death and illness, lost wages, financial losses to victims of substance-related crime who were hurt by others, combined with the cost of law enforcement activities directly aimed at the problem of SUDs, illicit and legal SUDs cost at least \$900 for every person 18 years or older in the United States each year (Heyman, 2009). When the cost of disability, accidental injuries, health care, and absenteeism from work are added together, the total economic impact of the SUDs on the U.S. economy each year is estimated

to be \$468 billion (CASA, 2012; Gonzalez, Vassileva, & Scott, 2009). The reasons for this huge economic burden can be seen in the facts that individuals who are hospitalized because of alcohol misuse had average hospital care expenses that were 120% higher than for persons who did not misuse alcohol, and that individuals who misuse opioids who are hospitalized require health care expenditures that are 482% higher than for those who do not misuse opioids (Santora & Hutton, 2008). Society's response to this crisis has arguably been haphazard, piecemeal, and frequently inadequate.

Who Treats Persons with an SUD?

Having established that SUDs are a legitimate problem, we are left with the question: Who treats those people with such disorders? The various state governments spend only two cents of every dollar on programs devoted to the prevention and treatment of persons with a SUDs (CASA, 2015; Grinfeld, 2001). Health care professionals in general are woefully ill-prepared to work with those who misuse substances. Although between 15 and 30% of patients seen by the typical primary care physician have an SUD, most physicians are still under-trained (or not trained) to recognize substance misuse (O'Brien, 2015; O'Connor, Nyquist, & McLellan, 2011). Less than one-fifth of physicians surveyed reported that they thought they were trained to treat patients with the most common form of SUDs, the AUDs, while less than 17% thought their training was sufficient to enable them to work with patients with other forms of SUDs (CASA, 2009a; Clay, Allen, & Parran, 2008). Only one medical school in the country requires a course on SUDs (O'Brien, 2015).

Further, most physicians emerge from graduate training with a negative attitude toward individuals with an SUD (Renner, 2004a). Possibly as a result of this deficit in their training and their preconceptions about persons with SUDs, fewer than one-third of physicians carefully screen for SUDs among their patients (Greenfield & Hennessy, 2008). Less than 50% of patients who go to see a physician about alcohol-related problems are even *asked* about their alcohol or drug use by their physician (Pagano, Graham, Frost-Pineda & Gold, 2005). This failure to inquire about patients' substance use habits might be a major reason why SUDs are both under-diagnosed and under-treated (Clay et al., 2008; Greenfield & Hennessy, 2008). This conclusion is supported by the observation that less than 1% of internal medicine and family practice physicians, and only 5.1% of psychiatric consultations, come to an accurate diagnosis of an SUD when it is present (Banta & Montgomery, 2007). Thankfully, there is a call to improve SUD training

for medical students across all fields of medicine (Das & Roberts, 2016; Ram & Chisolm, 2016).

Physicians are taught that addictions are chronic, treatable disorders, yet "more often than not [will] view the addicted patient as challenging at best and not worthy of customary compassion" (R. Brown, 2006, p. 5). Physician postgraduate educational programs have attempted to address this problem; however, the average length of such training in addictions is only about 8 hours (Renner, 2004a). Nor is this professional blindness limited to physicians. Nursing professionals frequently have more contact with patients than do physicians, yet "the majority of nursing schools . . . required only 1 to 5 clock hours of instruction on alcohol and drug abuse content during their entire undergraduate curricula" (Stevenson & Sommers, 2005, p. 15). Thus, those health professionals who will have the most contact with the patient—the nursing staff—are as ill-prepared to work with patients with SUDs as is the average physician.

Marriage and family therapists are another group of health care professionals who, as a whole, are ill prepared to recognize, much less deal with, SUDs. Such problems are rarely identified, meaning that vital clues to the nature of the disorder within the family are missed, and therapy might be rendered ineffective. If these disorders are identified, they are usually addressed by a referral to a therapist of another discipline than marriage or family therapy. This interrupts the continuity of care, and therapy is often carried out in a haphazard manner with little communication between researchers and clinicians (Batman & Miles, 2015) or between treatment professionals working with the same individual. Further, if there is a co-occurring disorder situation (SUDs with co-occurring mental illness) there is a definite need for family therapy, but this is rarely initiated (Minkoff, 2008).

Despite the obvious relationship between the SUDs and various forms of psychopathology, "most clinical psychologists are not well prepared to deal with issues involving substance use or abuse" (Sobell & Sobell, 2007, p. 2). Seventy-four percent of psychologists surveyed admitted that they had no formal training in the identification or treatment of addictions, and rated their graduate school training in this area as being inadequate (Aanavi, Taube, Ja, & Duran, 2000). Only professional substance abuse counselors are required to have a high level of professional training in the recognition and treatment of SUDs, with national standards for individuals working in this field having only recently been established. Since such counselors make up only a minority of those in the health care industry, the most common response to the question of who treats those individuals who are addicted to alcohol or drugs is all too often "nobody."


Designer Drugs for Pleasure: A (Frightening) Brave New World

There has been virtually no research into drugs whose purpose is to treat a disease but which induce a sense of pleasure or euphoria enjoyed by the patient (Morris, 2014). Pharmaceutical companies are now hard at work to correct this oversight, drawing upon the latest research into the manner in which the reward cascade works. It is impossible to predict when, but soon a new class of pharmaceuticals whose sole purpose is to induce a sense of pleasure in the user will appear on the market. The addiction potential of such chemicals is readily apparent, and raises a philosophical question: Does society have the right to block public access to such recreational chemicals? Would this not introduce a new class of illicit chemicals into society, setting the groundwork for the growth of illicit distribution networks such as those seen for

alcohol during the Prohibition era or the wave of methamphetamine use seen in the last decade of the 20th century and the first part of the 21st century? How should society respond to the hypothetical introduction of this new class of chemicals?

Chapter Summary

The problems of excessive alcohol use and illicit drug use have plagued society for generations. Solutions to the problem of the SUDs that have been shown to be inadequate include: banishment, execution, castration, incarceration, religious intervention, and various form of treatment. The United States, with a minority of the world's population, is the largest consumer of illicit drugs, yet society's response to the problem of SUDs has been poor at best, if not virtually entirely ineffective.



CHAPTER 2

The Nature of the Beast

(Being an Examination of the Problem of SUDs)

LEARNING OBJECTIVES

After reading this chapter you should be able to:

- 2.1 Understand why individuals may use alcohol and/or drugs
 - 2.2 Describe the cycle of drug misuse and the continuum on which individuals may fall
 - 2.3 Understand the terminology used in the field and in this text
 - 2.4 Consider the questions that remain unknown regarding SUDs
-

Introduction

Substance use disorders (SUDs) in the United States present the researcher in the field with a plethora of contradictions: laws made on the basis of prejudice, emotional reasoning, and preconception (Lachenmeier & Rehm, 2015); misinformation that sometimes reflects political agendas;¹ and a comparative lack of sound scientific research. One example of this might be seen in the extensive pool of data on the effects of pharmaceuticals, including therapeutic threshold, therapeutic and elimination half-lives, and side effects of compounds based on multi-participant research studies, and a lack of similar data on the drugs of misuse beyond what can be extrapolated from animal studies and anecdotal case reports.

The desire to become intoxicated is not unique to humans: Biologists have documented episodes in which at least some mammals appear to intentionally seek out fermented fruits or mushrooms that contain compounds that can bring about a state of intoxication. Many such episodes have been captured on film or electronic media and are available for viewing as public entertainment on the internet. Domestic cat owners have supplied their pets with catnip, often doing so on a regular basis, much to the delight of their four-legged family members. It would appear that we share the desire to chemically alter our perception of the world with our mammal cousins.

The American Society of Addiction Medicine (ASAM) has suggested a model of substance use disorders that attempts to integrate the biological, psychological, and sociological theories of addiction into one unified model.² This model attempts to address the various forces that

¹See discussion in Chapter 38 of how marijuana came to be criminalized, for example.

²Discussed in Chapter 26.

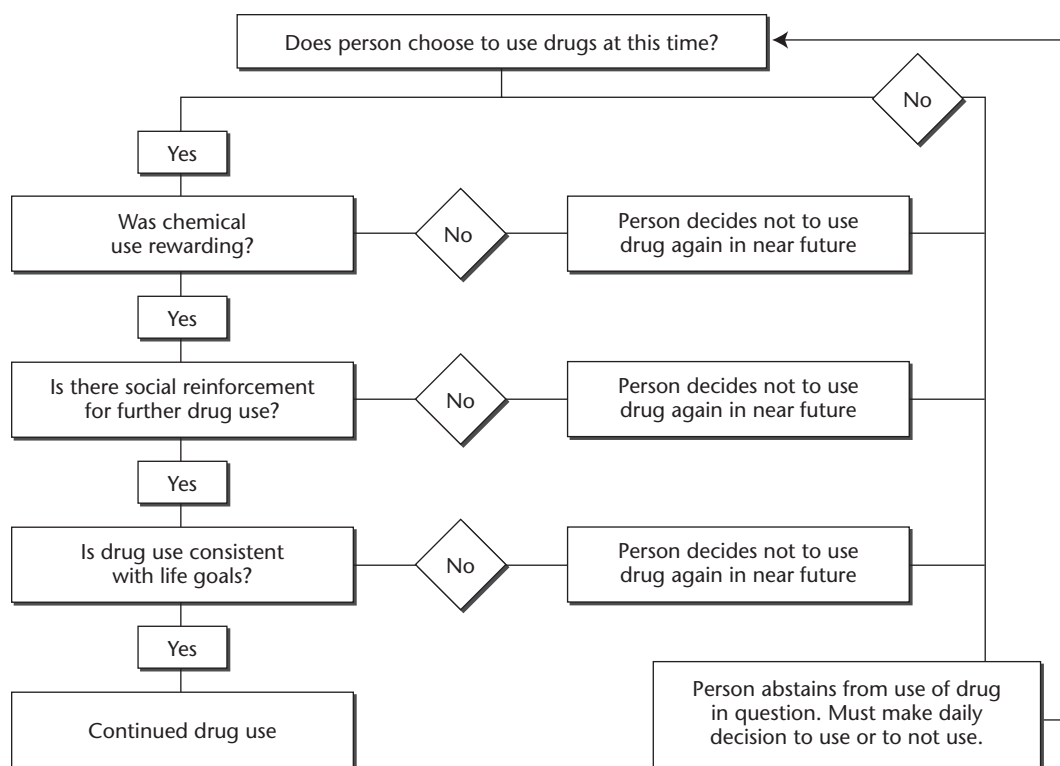


FIGURE 2-1 The Chemical Use Decision-Making Process.

exacerbate or inhibit an individual's substance use behaviors. While the current ASAM model is not the grand unified theory (or GUT) of addiction that has long been sought, it is a major step in the formulation of a GUT. However, until this grand unified theory is advanced, we are left with the question: What are substance use disorders and why are they a problem?

Why Do People Choose to Use Drugs or Alcohol?

There are many answers to this question, as substance abstinence, use, or misuse are common endpoints of the various forces that help to shape the individual's life and decisions. One individual might use chemicals to express a previously forbidden impulse, while another does so to cope with emotional or physical pain. Some choose to use chemicals to explore alternative realities, while others seek a substance-induced feeling of euphoria in place of the mundane reality in which they live. For some, substance use offers a way to escape from perceived injustices at the hands of fate, satisfy their curiosity about the effects of the chemical, or as a sign of rebellion, social connection, or simply for fun, just to mention

a few reasons a person might initiate substance use (Golub, Bennett, & Elliott, 2015; Rasmussen, 2008).

One factor that is frequently overlooked in the initiation or maintenance of substance use is *choice* (Hart, 2013). Every day we must make a conscious choice to use or not to use a recreational chemical or chemicals.³ A possible reflection of this decision-making process is seen in Figure 2-1.

Admittedly, for most of us this decision is so automatic that it does not even require conscious thought.⁴ However, whether on a conscious or unconscious level, we choose to engage in substance use or abstain. The decision to initiate substance use is influenced by a wide range of factors including:

Blindness to the compound's effects: When we use any compound, be it a pharmaceutical or illicit drug,

³In response to those of you who wish to argue this point, consider the following: Where is the nearest liquor store, or bar? If you wanted to do so, would you know where to buy some marijuana? If you did not know, would you know the name of a person to ask who would know? Are there certain people that you know of (coworkers, friends, etc.) whose company you avoid because you do not approve of their substance use? You see: We are not so removed from the problem of recreational drug use as we would like to believe, are we?

⁴The issue of choice in the initiation or maintenance of substance use will be discussed in Chapter 26.

we do so with certain expectations about that compound's effects. Individuals who use illicit drugs engage in the misuse of alcohol or drugs because they want to experience euphoria, increased coordination, or at least a reduction in tension. After taking such compounds, individuals will usually report that they *feel* better and are more capable of meeting the demands of life, although an unbiased observer might find evidence of increased interpersonal conflict, reduced ability to make appropriate financial decisions, cognitive dysfunction, and a reduction in the individual's ability to handle necessary activities of daily living (Breggin, 2008). Many individuals who misuse substances then interpret their experience with a drug(s) based on their expectations for that drug's effects even if the compound is technically incapable of meeting those expectations.

Pharmacological reward potential: The basic laws of behavioral psychology hold that if something (a) increases the individual's sense of pleasure or (b) decreases his/her discomfort, then s/he is likely to repeat the behavior (in this case, using alcohol or a drug). In contrast, if a compound were to (c) decrease the individual's sense of comfort or (d) reduce the individual's sense of pleasure, s/he would be less likely to repeat that behavior. While the drug that presents at least a moderate reward potential might be a powerful incentive for repeated use, it is not sufficient in itself to cause addiction to that compound (Kalivas, 2003). The drugs that are misused *are* drugs because they are able to induce pleasurable effects, or at least negate uncomfortable feelings such as anxiety and depression for short periods of time (Budney, Sigmon, & Higgins, 2003; O'Brien, 2006). The reward potential of these drugs is seen in the observation that they force the release of 2–10 times as much dopamine in the brain's reward system as do normal reinforcers (Lehne, 2013). The reward potential of a compound is, however, modified in part by its chemical structure, the individual's expectations, individual biochemistry, and the route of administration. Those compounds that have a rapid onset of action and which rapidly induce a sense of pleasure have the highest potential for misuse⁵ (Kalivas, 2003; O'Brien, 2011).

⁵Compare the abuse potential of a hypothetical compound that will induce a sense of pleasure in 4–5 minutes, as compared with that of a second hypothetical compound that will induce a sense of pleasure in 4–6 hours, and you will understand this point.

Social learning: The role of social learning is discussed in more detail in Chapter 26. It is mentioned here because: (a) drug misuse is a culturally defined phenomenon (Golub et al., 2015; Lehne, 2013), and (b) social learning is involved in the development of the individual's expectations for each potential recreational substance. Social learning is itself dependent on the accuracy of the information being presented to the individual. For example, many individuals who misuse opiates are inaccurately told that you cannot become addicted to a substance that you simply "snort." They believe this myth in part because friends often reinforce this misperception in spite of the libraries full of data that argue the exact opposite. Often, the price for this ignorance is the development of a physical addiction to what was at first a recreational substance for the individual.

Individual expectations: Substance use expectations begin to evolve in childhood or early adolescence, and evolve over time as a result of such influences as peer groups, childhood exposure to advertising, parental substance use behaviors, and learning (Monti et al., 2002; Sher, Wood, Richardson, & Jackson, 2005). The individual's expectations for a substance are also strongly influenced by the context and cultural traditions in which s/he uses that chemical (Lindman, Sjöholm, & Lang, 2000; Sher et al., 2005). The topic of how individual expectations about the effects of a substance overlaps the topic of learning theory, which is discussed in more detail in Chapter 26.

Cultural/social influences: Each individual lives in a cultural matrix that both helps shape his or her behavior, and is affirmed by that person's adherence to the norms. The topic of the social and cultural factors that influence substance use behaviors will be discussed in more detail in Chapter 26.

Legal sanctions: In today's society, the job of enforcing social rules is often carried out by the judicial system. If the individual should elect to use a drug(s) whose use is not approved of by society or to use a socially accepted drug in a manner that is not acceptable,⁶ the legal system steps in to punish this unacceptable behavior

⁶Even in this category, there are contradictions. For example, the recreational use of a narcotic is illegal, and a matter for the courts to handle. However, if the person were to have a prescription from a physician, s/he now becomes a "patient" for whom the use of the same compound is sanctioned.

(Szasz, 2009). However, the perspective of substance use disorders as reflecting a “disease” state, as advocated by the health care establishment, is often in conflict with that of the legal system, which adheres to the premise that the individual must be held accountable for his or her socially inappropriate behaviors, including the use of chemicals deemed unacceptable to society at large. This topic will be explored further in Chapters 37 and 38.

Drug Use/Misuse Cycles

Borrowing an analogy from infectious disease, Bennett and Golub (2012) suggested that the misuse of various compounds passes through several phases analogous to those seen in epidemics of infectious diseases: (1) *Incubation*: The misuse of a certain compound is infrequent within society, although it might be more popular with certain subgroups. Examples might be found in how marijuana was mainly limited to small segments of society (rebels, nonconformists, some musicians, etc.) before the 1960s, when it entered the second stage, (2) *expansion*: the misuse of the compound is more widely accepted, and a growing number of people try it at least once. Some of these individuals will continue to misuse the compound on an irregular basis, or go on to misuse the compound on a regular basis. During stage 3, the misuse of the compound reaches a *plateau*, with many who have used the compound choosing to discontinue the use of the compound at about the same rate that others initiate its use. Finally (4), the cycle reaches the stage of *decline*, with an ever-shrinking number of people initiating or continuing the misuse of the compound. This is not to say that the misuse

of the compound in question disappears entirely: There is always a small number of individuals who continue to use it, bringing the cycle back to stage one: incubation. This pattern has been seen with virtually every drug that is misused (Bennett & Golub, 2012).

The Continuum of Chemical Use

There is a great deal of confusion surrounding the terms *substance use*, *misuse*, *abuse*, and *addiction*. Terms such as *personality*, *addiction*, or even a *mood disorder* are not well defined scientifically (Churchland, 2013). Adding to the confusion are the facts that substance misuse is culturally and not scientifically defined, and that the frequency of substance use does not automatically indicate addiction (Golub et al., 2015; Hart, 2013; Lehne, 2013). For the sake of this text, substance use “is considered a normal learned behavior that falls on a continuum ranging from patterns of little use and few problems to excessive use and dependence” (Budney et al., 2003, p. 249).

Willenbring (2010) suggested that individuals who use alcohol fell into one of three categories: (a) normal drinkers (who never exceed the guidelines used to define normal drinking) (b) “at risk” drinkers (persons who exceed the guidelines but who currently do not have symptoms of alcoholism and have never met the diagnostic criteria for this condition), and (c) persons who meet the criteria for an alcohol use disorder. While useful, this continuum fails to include those persons who never drink, or who previously misused alcohol but do not now, or those who use illicit drugs. It also fails to show the continuum created by the alcohol use disorder diagnostic criteria. For this text, we will use the continuum shown in Figure 2-2 to examine substance use.

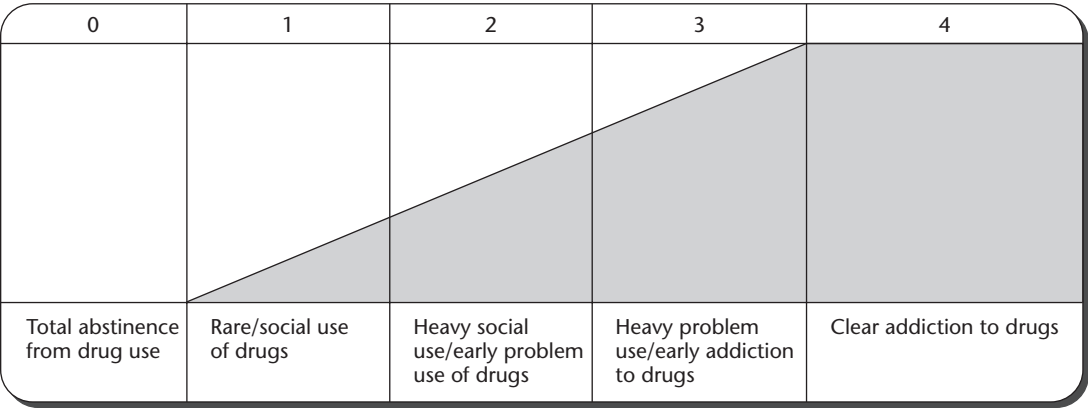


FIGURE 2-2 The Continuum of Recreational Chemical Use.

Admittedly, this continuum is an artificial construct, reflecting the lack of agreement among behavioral scientists about the definitions of such terms as “normal use” or “substance use disorder” (Churchland, 2013). This continuum has few clear demarcations between one stage and the next, and it should not be assumed that an individual using substances will automatically move from one stage to the next (Brust, 2004; Washton & Zweben, 2006). For example, 90% of those people who drink excessively are not actually addicted to alcohol (Esser et al., 2014). For the sake of this text the various stages are defined as follows:

Level 0: **Total abstinence** from all recreational chemicals.

Level 1: **Rare to social use** of recreational chemicals. This might include experimental use of a compound when the level of use does not exceed social norms.

Level 2: **Heavy social use/early problem use**: Although the majority of individuals who use substances moderately or control their use of chemicals (Bennett & Golub, 2012), some individuals fall into a pattern of substance misuse that is clearly above the social norm. Such individuals might experience limited legal, social, vocational, or medical consequences caused by their substance use. This does not automatically mean that the individual is *addicted* to that compound, only that their substance use pattern is beyond the norm and is causing social problems.

Level 3: **Late problem use/early addiction**: Individuals in this category may be physically dependent on a compound(s) and possibly also experience the classic withdrawal syndrome for the compound(s) being misused if they should abruptly stop using alcohol or their drug(s) of choice.⁷

Level 4: **Middle to late stage addiction**: Individuals whose substance use would fall in this category demonstrate all of the classic signs of addiction: physical, medical, legal, occupational, and/or personal problems, as well as a possible physical dependency on alcohol/drugs.

The continuum introduced above reflects the individual's *current* substance use pattern. Their substance use history might have been far different. For example, an individual might present a history of heavy substance misuse in the past but have abstained from all chemical use for the past 5 years. This temporal issue is a source of endless confusion for mental health professionals (Heyman, 2009). This dilemma is illustrated by the fact that up to 72% of

those persons who develop alcohol dependence will remain dependent on it for 3–4 years, after which time they either discontinue or at least significantly reduce their alcohol use (Heyman, 2009; Tucker & Simpson, 2011; Willenbring, 2010). A hypothetical college student who at the age of 20 met established diagnostic criteria for an alcohol use disorder might, a decade later, only be a rare social drinker now that he or she has work obligations, possibly a family, and most certainly bills to pay.⁸ Thus, there is the element of *time* that must be considered when assessing the individual's substance use pattern.

What Do We Mean When We Say That Somebody Is “Addicted” to a Chemical?

There is a wide discrepancy between how the average citizen defines “addiction” and what health care professionals mean when they use the same word (Szalavitz, 2010). Physical dependence on a substance is one of the traditionally accepted signs of addiction (O'Brien, 2011); however, physical dependence on a compound is not *automatically* a sign of addiction⁹ (Lehne, 2013). There are simply no universally accepted definitions of the terms *problematic use*, *abuse*, or *addiction* (Churchland, 2013; Wunsch, Boyd, & McMasters, 2009). In the case of alcohol, *excessive use* is not automatically a sign of addiction: The team of Esser and colleagues (2014) found that only about 10% of individuals who drank alcohol to excess met the criteria for *alcohol dependence*. To assist in diagnosing substance use issues, medical professionals use lists of standardized diagnostic criteria, such as those outlined by the American Psychiatric Association's (2013) *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5). These criteria, updated from the two categories of substance abuse and substance dependence in the previous version, add additional challenges, with the changing of terminology not only within the professional setting, but within research as well. The specific criteria identified in DSM-5 can be grouped into four general categories (American Psychiatric Association, 2013):

1. Impaired control over substance use,
2. social impairment due to substance use,
3. use of substance under risky circumstances,

⁸College loans leap to mind here, although other financial obligations might include a mortgage on a house, car loans, home remodeling costs, etc.

⁹For example, a patient might become habituated to the use of a compound being used to treat an illness, but this is not a sign of addiction to that compound.

⁷The claim “I can stop any time that I want to!” might be a motto for individuals whose substance use falls in this category.

4. pharmacological effects of the drug(s) on the individual, including the development of tolerance and withdrawal symptomology.

There are specific diagnostic criteria for each substance identified in the *DSM-5*. The reader is referred to the *DSM-5* for more information about the specific diagnostic criteria for each drug category. This is not the only classification system in use. The *International Classification of Diseases* is another such system, with the 11th edition available in 2018. The 10th edition is widely used by insurance companies in the United States and in other countries, and unfortunately is not entirely compatible with the *DSM-5*, which is a major shortcoming of the *DSM-5* classification system.

The two diagnostic systems share certain common elements: (1) the view that it is a primary disease; (2) it has multiple manifestations in the person's life, including the social, psychological, spiritual, vocational, interpersonal, and economic spheres of their lives; (3) it is often progressive; (4) it is potentially fatal; (5) it is marked by the individual's inability to control (or at least to consistently control) their substance use; (6) it is marked by preoccupation with drug use; (7) the individual develops a distorted way of looking at the world so that it supports his/her continued use of the compound(s); (8) the individual becomes tolerant to the effects of the compound(s), and s/he either must go through "drug holidays" in which s/he loses some of the tolerance to the substance, or must use larger and larger amounts in a manner designed to overcome his/her tolerance; and finally, (9) the individual will experience a characteristic withdrawal syndrome if s/he should discontinue use of the compound(s).

Definitions of Terms Used in This Text

At this point it is necessary to establish a common language so that we are "all on the same page," so to speak. Thus, for the sake of this text, the following definitions will be used:

Social Use: A point of confusion is that use of a substance is equated with a substance use disorder, especially when a person is using illicit drugs. However, "being a substance user does not mean invariably that one has a substance use disorder" (Gonzalez, Vassileva, & Scott, 2009, p. 456). The individual's culture defines the frequency with and conditions under which an individual might use a substance(s). Currently, alcohol, tobacco,

and in some states marijuana are the only products that might legally be used in certain social settings.¹⁰

Substance Abuse is the term that has been used when an individual uses a compound when there is no legitimate medical need to do so, or when the compound is used in excess of social standards (Schuckit, 2006a, 2006b). There is no physical dependence on the chemical(s) in question at this time, and it does not automatically progress to physical addiction to the compound (Swift, 2005). However, given the frequent confusion that arises from use of the term substance abuse, including confusion resulting from its previous inclusion as a diagnostic category as discussed earlier, the term *substance misuse* will be used instead of substance abuse in this text. This change is consistent with the move by the Office of National Drug Control Policy (2006) to reduce stigma, which also includes the push to use what is called *person-first language*, that is, referring to the person first, such as an individual with a substance use disorder, or an individual who misuses substances, rather than a substance abuser or addict.

Drug of Choice: Clinicians once spoke about the individual's *drug of choice* as an important component of the disease of addiction. Indeed, this was the reason Narcotics Anonymous was founded: Individuals who used illicit drugs and who attempted to join Alcoholics Anonymous (AA) in the 1950s and 1960s were told that they could only talk about their alcohol use disorder at meetings because AA was not intended to address drug addiction, only alcoholism. With the growth of polydrug¹¹ disorders, the concept of drug of choice has fallen into disfavor and few clinicians now place emphasis on this concept. Zuckerman (2012) suggested that the individual's search for novel sensations is the strongest predictor of the number of drugs a person misuses. However, the *availability* of alcohol and the various drugs also shapes the individual's substance use pattern.

Loss of Control is a poorly defined term. In essence, a person who cannot accurately predict in advance how much alcohol or drug(s) he or she will use on any given occasion might be said to have lost control

¹⁰An excellent example of how cultural norms govern substance use.

¹¹Or "multi-substance" use issues.

over his or her substance use. An example might be that a person who intended to have “just one or two drinks” with friends, only to drink to the point of gross intoxication within hours could be said to have demonstrated a loss of control over his alcohol use.

Addiction/Dependence: These are also poorly defined terms, and will generally be avoided in this text. Many clinicians use the term *dependence* on a chemical, although some professionals still use the term *addiction* to refer to the more severe end of the spectrum of SUDs, despite the removal of the term from the *DSM-5* terminology (APA, 2013). Dependence was previously said to exist when the individual met the DSM-IV criteria for alcohol or drug dependence, as discussed in the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.) (American Psychiatric Association, 2000). Dependence is marked by the development of a characteristic *withdrawal syndrome* for compound(s) being misused that have not been prescribed. If the drug was prescribed by a physician for the treatment of a disease state, the same process is called *neuroadaptation*. This process will be discussed in more detail in the next chapter.

Tolerance to a drug(s) is said to develop when the individual must use more of a compound to achieve the effects once achieved at a lower dose. Some of the more significant subforms of tolerance will be discussed in more detail in the next chapter.

Withdrawal Syndrome is a phenomenon experienced when the individual either stops, or significantly reduces, his or her intake of a specific compound. The withdrawal syndrome is usually the opposite of the compound's effects on the user's body. Thus, for example, alcohol acts like a chemical “brake” on the neurons of the brain. The neurons struggle to compensate, increasing the number of neurotransmitter receptor sites for excitatory neurotransmitters to overcome the inhibitory effects of the persistent alcohol use. When the individual with a severe AUD stops drinking, this “brake” is removed, and neurons in the brain might become overactive. This is experienced by the individual as anxiety, withdrawal tremors, and in extreme cases delirium tremens (DTs), all of which are discussed in more detail in later chapters.

The world of the addictions is replete with a range of other terms that serve as a form of professional shorthand for

individuals who work in the field, but the above terms should serve as a solid foundation from which the reader can begin to understand the world of substance use disorders. It is important to realize how other professionals as well as individuals encountered while conducting professional work use such terms. Thus, being clear on one's own definitions, as well as being careful to not make assumptions about the definitions other professionals may be using (as well as patients, clients, etc.), is essential to “being on the same page” in the settings readers may be or may soon be operating in.

Behavioral/Process “Addictions”

For the last quarter of the 20th century, a fierce debate raged over the question of whether such things as sex, food, men, women, play, shopping, shoplifting, carbohydrates, unhappy relationships, french fries, lip balm, credit cards, etc. could be said to be an “addiction” (Barber, 2008; Jaffe & Anthony, 2005). There is little physical evidence at this time that non-drug centered behaviors can result in a physical addiction; clinicians are increasingly classifying these behaviors as “behavioral addictions” or compulsive behaviors as opposed to substance use disorders (Fong, Reid, & Parhami, 2012). However, some research indicates that SUDs and gambling disorder both relate to the dopamine pathways and within the same areas of the brain (Grant, Potenza, Weinstein, & Gorelick, 2010), and that internet addiction has a similar impact on neural pathways (Love, Laier, Brand, Hatch, & Hajela, 2015). Although there are similarities with the SUDs, there are also numerous differences (Alavi et al., 2012). These behavioral addictions will not be discussed further in this text, as the focus is on substances in particular. However, a wise student will seek further research and training in the area of these behavioral/process addictions.

Unanswered Questions

If you were a devotee of the television talk shows, or read a small sample of the self-help books available, you would easily be left with the impression that researchers have discovered all that there is to be known about the cause(s) of and treatment(s) for substance use disorders. Unfortunately, *nothing could be further from the truth!* Much of what is “known” about SUDs is based upon mistaken assumptions, distorted data, clinical myth, theory, or, in many cases, incomplete data. Although few research studies identify the difference, the *lifetime* prevalence, which is to say whether a person has used a given chemical at *any* point in his or her life, differs from the *period* prevalence, that is, whether the

individual has used a given chemical during a specified period of time (usually one year) (Brook, Pahl, & Rubenstone, 2008; Wakefield & Schmitz, 2014). In many research studies, the two groups are lumped together as if they were a uniform group of individuals.

The folly of this perspective is seen in the fact that at some point in their adult lives perhaps 30–45% of all adults will demonstrate at least one sign of an alcohol use disorder (alcohol-related “blackout,” legal problem, etc.). This does not mean that 30–45% of the adult population of this country is or will become alcohol-dependent! Most people either use alcohol socially, or, upon encountering a sign of a serious alcohol use disorder, abstain from further use. Additionally, professionals struggle to determine who truly needs treatment, as many “false positives” are created because of the diagnostic criteria used and the broad continuum that results (Wakefield, 2015, p. 188). Neither clinical researchers nor substance rehabilitation professionals know how to identify the individual who will go on to develop a serious alcohol use disorder¹² from the one who will experience a transient substance use problem, in spite of public displays of confidence.

An inconvenient truth is that there are earnest questions that face researchers in the field of the addictions:

1. Are those individuals who seek treatment the same as those who do not?
2. Are those individuals who occasionally use drugs different in some poorly understood way from those individuals who go on to become physically dependent on a drug or alcohol?
3. Is research carried out on those individuals who seek treatment through the Veterans Administration hospital system applicable to the general population?
4. How do men and women who have SUDs differ? Do the same treatment techniques work for each subgroup?
5. Are those individuals who misuse substances and who hold full-time employment the same as or different from those individuals who misuse substances who do not hold full-time jobs, and are individuals in either group the same as or different from those who are unemployed?
6. Are those persons who limit their substance use to alcohol the same as those who use an illicit drug, or who use multiple drugs?
7. It is known that the individual’s motivation for substance use varies as a result of his or her age and past

substance use history. How do these variables affect the processes of intervention and rehabilitation?

8. What is the contribution of the individual’s genetic heritage to the development of an SUD, and how is this genetic heritage modified by environmental forces?

It is difficult to answer these and a host of other questions, in part because much of the clinical literature addresses only the alcohol use disorders (AUDs). There are probably differences between persons with an AUD and persons with an opioid use disorder, to cite one possibility, but there is a dearth of clinical research into such differences. The assumption that the forces that shape SUDs in men automatically are the same as those that apply to women has also been challenged.¹³ As will be discussed in Chapter 20, the problem of child and adolescent substance misuse has virtually been ignored until recently, and much of what was thought to be “known” about this problem reflected assumptions based on adult populations.

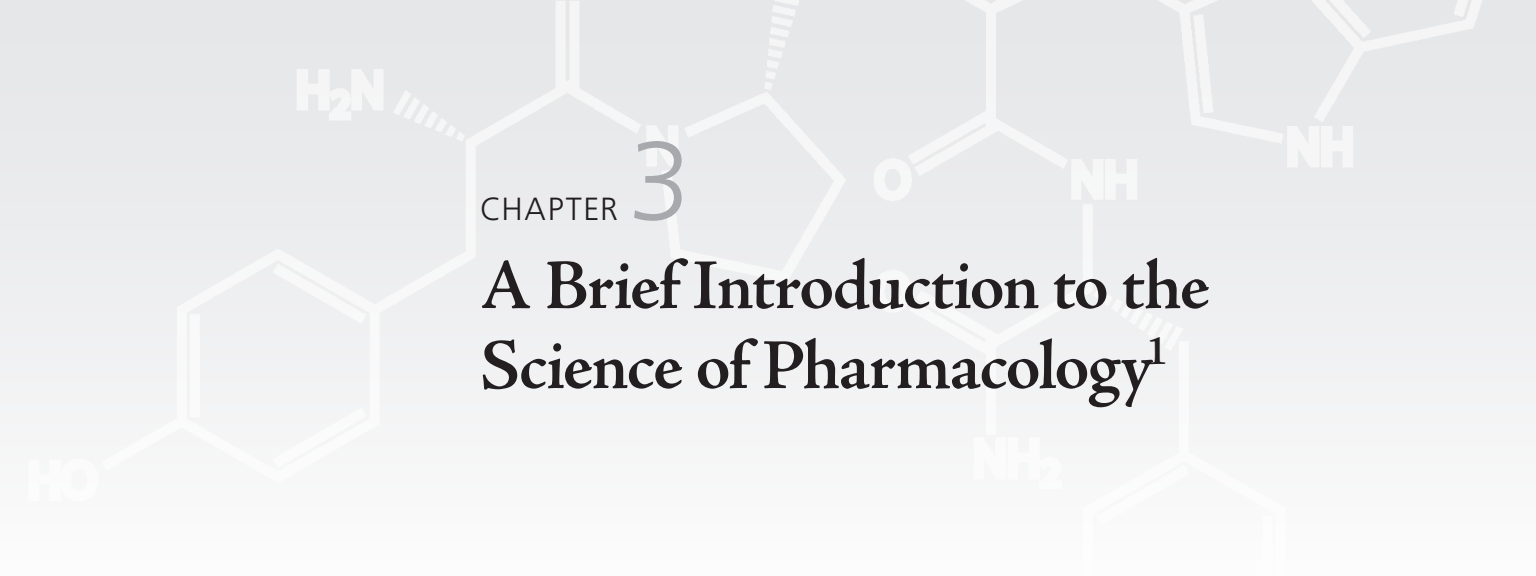
Thus, much of what we think we know about substance use disorders is not based on scientific research, but on assumptions, guesses, and limited data. However, it is on this foundation that an entire rehabilitation “industry” has been based. It is not the purpose of this text to deny that SUDs exact a terrible cost in individual suffering and to society, but hopefully the reader has started to understand how little is really known about the substance use disorders.

Chapter Summary

In the end, the “nature of the beast” remains elusive and unclear. Only the foundations of understanding have been established, as reflected by the basic concepts used by researchers and clinicians who work in the field of substance rehabilitation, as discussed in this chapter. Although many view SUDs as black-and-white conditions (either the person is addicted or not), the fact that a person’s substance use behavior exists on a continuum and that their place on that continuum might change over time was discussed. This chapter also established parameters for terms such as *substance use*, *misuse*, and *addiction*, as used in this text, to establish a common language. The more pertinent elements of the American Psychiatric Association’s (2013) *Diagnostic and Statistical Manual for Mental Disorders*, 5th edition, were reviewed. Some of the forces that contribute to the development of an SUD were introduced, and will be discussed in more detail in later chapters. Unanswered questions facing mental health professionals in their quest to better understand SUDs were raised, as was the fact that there is still a great deal to learn about SUDs.

¹²Alcohol use disorders (AUDs) are a subset of substance use disorders. When the discussion is limited only to alcohol, the terms *alcohol use disorders* or *AUDs* will be used. When the topic is limited to cocaine use or addiction, the term *cocaine use disorders* will be used, etc.

¹³See Chapter 18.



CHAPTER 3

A Brief Introduction to the Science of Pharmacology¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 3.1** Understand the impact substances can have on the body
 - 3.2** Distinguish prime effects from side effects
 - 3.3** Describe the forms of administration of substances
 - 3.4** Understand the factors that impact the bioavailability of substances
 - 3.5** Distinguish between the different types of half-lives for substances
 - 3.6** Describe the difference between effective dose and lethal dose
-

Introduction

It is virtually impossible to discuss the effects of the various drugs without touching on a number of basic pharmacological concepts. Although a complete understanding of the science of pharmacology can take years to attain, in this chapter we will discuss the impact that the various drugs that are misused might have on the individual's body, and the pharmacological principles by which these effects take place. To frame the discussion, it is important to realize that pharmacology is often discussed in terms of **pharmacokinetics** and **pharmacodynamics**, the first being how time impacts a drug moving through the body, and the second being the way in which a drug impacts the body, including for how long and how strong (DeVane, 2017).

A Basic Misconception

It is surprising how often people discuss illicit drugs as if they were somehow a special class of chemicals that are unique. In reality, most of the drugs that are misused were used as pharmaceutical agents in the past, and of those that were not actual pharmaceuticals, many were investigated as possible medications. Thus, they work in the same manner that the other pharmaceuticals do: by changing the biological function of target cells through chemical actions. As is true for most

¹This chapter is designed to provide the reader with a brief overview of some of the more important principles of pharmacology. It is not intended to serve as, nor should it be used for, a guide to patient care.

of the pharmaceuticals in use today, drugs that are misused strengthen or weaken a potential that already exists within the body. In the case of drugs individuals are intending to misuse, the target cells are usually in the central nervous system.

The Prime Effect and Side Effect of Chemicals

It is often surprising for students to learn that it is virtually impossible to develop a mind-altering drug without unwanted side effects. This is “because the brain is so highly integrated, it is not possible to circumscribe mental functions without impairing a variety of other functions, typically causing generalized dysfunction of the brain and mind” (Breggin, 2008, p. 2). Side effects often extend beyond the brain, such as the constipation so often experienced with use of opioids (Gudin, Laitman, & Nalamachu, 2015). Thus, in order to achieve the **prime effect**² of a compound, the user must endure the **side effects**³ of that compound as well. Some of these side effects will be relatively minor, while others might be life-threatening. This rule holds true both for pharmaceutical agents prescribed by a physician for a patient and for the drugs that are misused.

For example, a person might ingest a dose of aspirin to help him or her cope with the pain of a minor injury. However, aspirin also has an anticoagulant side effect, inhibiting the body’s ability to form blood clots if necessary.⁴ This anticoagulant effect increases the individual’s risk for excessive bleeding either at the site of the original injury or at the site of a second injury to the unlucky victim. Another example of the difference between the primary and side effects of a medication is seen in the patient who has developed a bacterial infection in the middle ear (a condition known as *otitis media*) and who is prescribed an antibiotic such as amoxicillin. The desired effect is the elimination of the offending bacteria in the middle ear, but an unwanted side effect might also be the death of bacteria in the gastrointestinal tract, where those bacterial strains assist in the process of digestion. The point to keep in mind is that there are the desired primary effects and unwanted side effects, or what are also known as **secondary effects**, to every compound. The side effects can

range in intensity from mild discomfort to life-threatening conditions.

The Method by Which a Compound Is Administered

One factor that influences the intensity of a drug’s primary and side effects is the manner in which it is administered. Another factor is that the specific *form* in which a compound is administered will have a major impact on (a) the speed with which the compound begins to have an effect on the body, (b) the way that the compound is distributed throughout the body, (c) the intensity of its effects, and (d) the speed with which the individual will begin to experience any side effects from the compound. Kamienski and Keogh (2006) identified 13 different ways that a compound could be introduced into the body, whereas other authors identify upwards of 20 routes of administration (Turner, Brabb, Pekow, & Vasbinder, 2011). Fortunately, most of the drugs that are misused are administered either by the **enteral** or the **parenteral** route.

Typical Forms of Drug Administration

Compounds administered by the enteral route enter the body by the gastrointestinal tract and usually are administered in oral form (Jenkins, 2007; Lehne, 2013; Williams & Baer, 1994). The most common form of enteral drug administration is in tablet form, which is essentially a selected dose of a compound mixed with a binding agent that acts to give it shape and hold its form until it enters the gastrointestinal (GI) tract. In most cases, the tablet is designed to be ingested whole, although in some cases it might be broken up to allow the patient to ingest a smaller dose of the medication or for ease of administration, if desired. Once in the GI tract, the compound begins to break down and separate from the binding agent and is absorbed through either the stomach or the small intestine.

Another common method of oral medication administration is the capsule. This is a modified form of tablet, with the medication being suspended in a solution and surrounded by a gelatin capsule. The capsule is swallowed whole, and, once it reaches the GI tract, the gelatin capsule breaks down, allowing the absorption of the desired compound. Some compounds are simply administered as liquids, such as children’s medication(s). This allows for titration of the dose according to the child’s weight. On rare occasions, medications are administered to adults in liquid form, and it

²See Glossary.

³See Glossary.

⁴This anticoagulant effect makes aspirin of value in preventing the formation of blood clots that might eventually cause a heart attack or stroke, and for breaking up blood clots that have already blocked key blood vessels in the heart.

is not uncommon for **over-the-counter medications**⁵ and, less commonly, illicit drugs to be administered in liquid form.

A number of compounds might be absorbed through the blood-rich tissues found under the tongue. A chemical that is administered in this manner is said to be administered **sublingually**, which is a variation of the oral form of drug administration. Some of the compounds administered sublingually include nitroglycerin and buprenorphine. The sublingual method of drug administration avoids the danger of the “**first-pass metabolism**” effect (discussed later in this chapter) (Jenkins, 2007). However, in spite of this advantage, the sublingual form of drug administration is only rarely used, although buprenorphine is frequently used by individuals struggling with opioid use disorders (Rosenthal et al., 2016).

While many compounds are rapidly absorbed rectally, this method of drug administration is uncommon in medical practice, and it used to be virtually unheard of in those who use illicit drugs (Jenkins, 2007). Rectal drug administration has been seen with newer drugs (such as “flakka”; Katselou, Papoutsis, Nikolaou, Spiliopoulou, & Athanaselis, 2016) as well as alcohol (Stogner, Eassey, Baldwin, & Miller, 2014), although it is still quite rare.

The parenteral method of drug administration involves the injection of a compound directly into the body. There are several advantages to parental forms of drug administration, including the fact that the drugs are not exposed to gastric juices, delays caused by the stomach emptying process, or the danger of being mixed with food in the GI tract, which might delay absorption. It also avoids first-pass metabolism. Depending on the substance being discussed, the intravenous administration of that chemical might be the preferred method of administration, especially when a rapid onset of effects is desired. However, the **subcutaneous** method of drug administration is not unheard of. This involves the injection of the compound just under the skin, allowing for a reservoir of the drug to be established in the body and a slower rate of absorption than the intravenous administration method. This is often a method by which illicit narcotics are first injected, and is referred to as “**skin popping**” by those who use illicit drugs.

Another method of parenteral drug administration involves the injection of a compound(s) into muscle tissue (**intramuscular** or IM injection). Muscle tissues have a good supply of blood, and many compounds injected into muscle tissue will be absorbed into the general circulation more rapidly than compounds injected just under the skin. This method of drug administration is used both for the

administration of some pharmaceuticals in medical practice and sometimes by those who use illicit drugs, such as those who inject the anabolic steroids. However, there are many compounds such as benzodiazepine chlordiazepoxide (used with acute alcohol withdrawal) that are poorly absorbed by muscle tissue, and are thus rarely if ever administered by this route (DeVane, 2004, 2017).

Intravenous (or IV) injection is a frequently used method of drug administration. In this process, the compounds of choice are injected directly into a vein, and are thus deposited directly into the general circulation (DeVane, 2004, 2017). This is a common method by which legitimate pharmaceuticals, and many illicit drugs, are administered. One serious disadvantage of the intravenous method of drug administration is that it does not allow the body very much time to adapt to the foreign chemical, and thus the individual is at risk for a serious adverse reaction to the compound within seconds of it being administered.

There are a number of additional forms of drug administration, which will only briefly be discussed in this text. The **transdermal** method of drug administration involves a compound being slowly absorbed through the skin. This has the advantage of allowing a low, but relatively steady, blood level of the compound(s) in question being established in the individual's body. This method of drug administration does not allow for one to rapidly establish any significant blood level of a compound in the body. For example, transdermal nicotine patches might require up to 24 hours before a sufficient level of nicotine is established in the person's blood to block nicotine withdrawal symptoms.

Another method of drug administration, one that is used more frequently by those who misuse drugs than in medical practice, is the **intranasal** method. In this method of drug administration, the compound is “snorted,” depositing it on to the blood-rich tissues in the sinuses. Cocaine and heroin powder, as well as methamphetamine, are often used in this manner. This allows for a relatively rapid absorption of the drug(s) in question, but the absorption rate is often erratic and slower than the intravenous route of administration. The process of snorting is similar to the process of **inhalation**, which is used both in medical practice (such as an inhaler for asthma or anesthetic gases used for surgery) and with certain compounds by those who misuse drugs. The process of inhalation takes advantage of the fact that the circulatory system is separated from direct exposure to the air only by a layer of tissue less than 1/100,000th of an inch (0.64 micron) thick (Garrett, 1994). Many drug molecules are small enough to pass across this barrier relatively easily, entering the individual's circulation quickly. Many of the drugs that are misused become able to cross over this

⁵See Glossary.

barrier if smoked, rapidly gaining access to the circulation. These compounds include heroin, methamphetamine, and cocaine. Finally, in the case of some compounds, the process of inhalation is able to introduce small particles into the deep tissues of the lungs, where they are deposited. These particles are rapidly broken down into smaller and smaller units until they are small enough to pass through the tissue barrier of the lungs into the circulation. This is the process that takes place when tobacco cigarettes are smoked, for example.

Each subform of inhalation takes advantage of the fact that the lungs offer a blood-rich, extremely large surface area, allowing for the rapid absorption of many compounds (Jenkins, 2007; Lehne, 2013). However, many factors influence the amount of a given compound that actually is absorbed into the general circulation, including: (1) The individual must inhale the compound(s) at exactly the right point in the respiratory cycle to allow the drug molecules to reach the desired point in the lungs, and (2) some chemicals are able to pass through the tissues of the lung into the circulation more rapidly than others because of the chemical structure of the molecule. Marijuana is a good example of this problem: The individual must hold his/her breath for as long as possible to allow the largest percentage of the molecules inhaled to cross into the circulation before the person must exhale.

Bioavailability

To have an effect, a compound must enter the body in sufficient strength to achieve the desired effect. This is referred to as the **bioavailability** of a compound. Essentially the bioavailability of a compound is the *concentration of unchanged chemical at the site of action* (Bennett & Brown, 2003; Xu, 2016). The bioavailability of a compound, in turn, is affected by the factors of (Bennett & Brown, 2003; Jenkins, 2007; Xu, 2016) absorption, distribution, biotransformation, and elimination. Each of these processes will be discussed in more detail, below.

Absorption

Except for topical agents, which are deposited directly on the site of action, such as an antifungal cream, most compounds must be absorbed into the body to have any effect (Jenkins, 2007; Lehne, 2013). This involves the drug molecules moving from the site of entry through various cell boundaries to the circulatory system, where they are transported to the site of action. Compounds that are weakly acidic are usually absorbed through the stomach lining, while compounds that are weak bases are absorbed in the small intestine (Jenkins, 2007; DeVane, 2004).

The human body is composed of layers of specialized cells, organized into specific patterns that carry out designated functions. The cells of the circulatory system are organized to form tubes (blood vessels), which contain the cells and fluids collectively called “blood.” Each layer of tissue that a compound must pass through in order to reach the circulatory system will slow absorption that much more. For example, as noted earlier, the circulation is separated from the air in the lungs by a single layer of tissue (the cell walls of the individual alveoli). Compounds that are able to cross this one-cell layer are able to reach the general circulation in a matter of seconds. In contrast to this, a compound that is ingested orally must pass through the layers of cells lining the GI tract and the blood vessels that surround it before it reaches the circulation. Thus the oral method of drug administration is recognized as being much slower than inhalation, for example.

There are a number of specialized *cellular transport mechanisms* which the body uses to move necessary substances into/away from the circulatory system. Drug molecules can take advantage of these transport mechanisms to move from the site of administration to the site of action. Without going into too much detail, it is possible to classify these cellular transport mechanisms as being either *active* or *passive* means of transport (Jenkins, 2007; Lehne, 2013; DeVane, 2017). The most common method by which drug molecules move across cell membranes is called diffusion, a passive method of molecular transport. Active methods involve the drug molecule taking advantage of one of several natural molecular transport mechanisms that move essential molecules into various cells.

The process of drug absorption is variable, depending on a number of factors, the most important of which is the *method of administration*, as discussed earlier in this chapter. Another major variable is the *rate of blood flow* at the site of entry. For example, an intramuscular injection into the deltoid muscle of a person suffering from hypothermia will result in poor absorption, since the blood has been routed to the interior of the body to conserve body heat. Under these conditions, the muscle tissue will receive relatively little blood flow, and this will reduce the speed at which the drug molecules injected into muscle tissue(s) might be absorbed into the general circulation.

Yet another variable is the *molecular characteristics of the compound itself*. Some drug molecules are more easily absorbed than others. Also, if the compound is administered orally, a factor that affects absorption of that drug is whether it is ingested on an empty stomach or not (DeVane, 2004, 2017). Most compounds are better absorbed when ingested on an empty stomach, although some others are

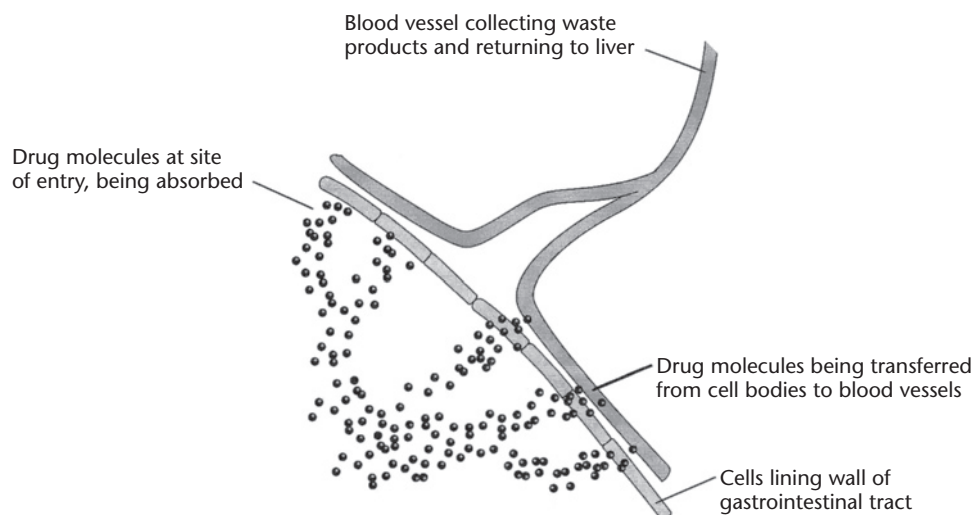


FIGURE 3-1 The Process of Drug Absorption.

better absorbed if ingested right after a meal (DeVane, 2004, 2017; Lehne, 2013). Further, one compound might best be absorbed if it does not have to compete with other drug molecules for admission into the body. All of these factors limit the absorption of some compounds into the circulation.

Distribution

The process of *distribution* refers to how the molecules of a chemical are spread in the body. This includes both the process of drug transport and the pattern of drug accumulation within the body. Very little is known about drug distribution patterns of certain chemicals, especially if the individual has overdosed on one or more compounds (Jenkins, 2007). The process of distribution is also affected by factors such as the individual's age, sex, muscle/adipose tissue ratio, state of hydration, genetic heritage, and health (DeVane, 2017). Because of such factors, there is significant inter-individual differences in the distribution pattern of the same compound at the same dosage level (DeVane, 2004, 2017; Jenkins & Cone, 1998).

Transport

Once the drug molecules reach the general circulation, they can then be transported to the site of action. Some chemicals are able to mix freely with the blood plasma, and as such are often referred to as **water-soluble** compounds. Much of the human body is water, so this provides a fine medium by which a water-soluble compound might be suspended and pumped around the body. Alcohol is a fine example of a

water-soluble compound, which, after absorption, becomes intermixed with the blood plasma and pumped through the body by the circulatory system. The characteristics of some drug molecules allow them to bind to one of the fat molecules that circulate through the body. Such compounds are called **lipid-soluble** or **lipophilic** compounds. The organs of the human body range from 6 to 20% lipid molecules, which are used for a variety of purposes, including maintenance of cell walls. Any drug molecule that has attached itself to a lipid molecule will then be dragged along as the lipid molecule circulates. Body tissues are constantly absorbing lipid molecules from the circulatory system as part of the cellular maintenance process, allowing lipid-binding molecules attached to the lipid molecules relatively rapid access to body tissues.

It is important to keep in mind some characteristics of molecular binding. First, as will be discussed in more detail later, the drug-molecular "binding" is usually not permanent. While the drug molecule is bound to the lipid molecule, it is safe from elimination from the body, but it is also unable to achieve its desired effects. To become active again, it must detach from the lipid molecule. To say that a compound is 98% lipid-soluble means that 98% of the drug molecules absorbed into the circulation are bound to blood lipids, leaving just 2% of the drug molecules to be biologically active. There are advantages and disadvantages to this characteristic of lipid binding. The process of lipid binding provides a drug reservoir within the body, as drug molecules detach from the lipid molecule over time. This allows new drug molecules to become active to replace those that have been eliminated from the body. However, the lipid-bound drug molecules

are unable to have an effect until they detach from the blood lipids.

Between 6 and 20% of the tissues that form the body are lipid molecules. An exception to this is the brain, which is 50–60% lipid molecules (Cooper, Bloom, & Roth, 2003; Glick & Fischer, 2013). A compound that is lipid-soluble will thus become concentrated in the brain. The ultra-short and short-acting barbiturates⁶ are excellent examples of this process. Some forms of the parent barbiturate molecule are able to form bonds with blood lipids very rapidly, thus allowing them to take advantage of the brain's constant demand for lipid molecules to reach the brain rapidly and take effect. In contrast to the lipid-binding compounds, some drug molecules might bind to one of the protein molecules that circulate throughout the body in the circulation.⁷ Drug molecules differ in their ability to bind with protein or lipid molecules. The antidepressant amitriptyline is 95% protein-bound, for example, while nicotine is only 5% protein-bound (Jenkins, 2007).

As with the process of lipid binding, some drug molecules form stronger bonds with the protein molecule than do others, and this is one factor that determines how long a given compound will remain in the body. As is true for lipid-bound molecules, protein-bound drug molecules are unable to have any biological effect as long as they remain bound to the protein molecule. It is important to keep in mind that drug molecules are foreign substances, and their presence in the body is only tolerated by the body until its natural elimination/defense mechanisms are able to latch onto and remove them. Thus, there is a constant process of drug molecule replacement during the period of active dosing, as some molecules are eliminated from the body and others break their bonds with the protein/lipid molecules and replace those that have been eliminated.

The number of binding sites on protein molecules is limited. If an individual were to take an unusually large dose of a drug, or if the molecules of more than one compound were competing for the same binding sites on the protein or lipid molecule, those binding sites would rapidly become saturated, leaving a larger than normal percentage of drug molecules free in the blood to have a biological effect. This is one of the mechanisms through which pharmaceuticals might have a **synergistic**⁸ effect: The effects of one compound may

reinforce the effects of a second compound, possibly with fatal results. Another form of synergistic effect is seen when different drug molecules bind at the same receptor site, increasing (or decreasing) the rate at which that neuron can “fire.”

Biotransformation

The biotransformation mechanisms in the human body have evolved over millions of years to help the organism deal with potentially dangerous chemicals found in foods that have started to spoil (Wynn, Oesterheld, Cozza, & Armstrong, 2009). In humans, these defensive detoxification systems are nonselective, eliminating poisons found in food with the same enthusiasm that they eliminate prescribed medications, since drug molecules are as foreign to the body as are poisons. In some cases, the body is able to simply filter the drug from the blood. Penicillin is an excellent example of such a compound. The penicillin molecules are filtered from the blood by the kidneys almost immediately. With the proper equipment it is possible to filter penicillin from the urine of a patient taking this compound, purify it and reuse it.⁹ There are other compounds which are removed from the body unchanged. However, in the majority of cases the chemical structure of the drug(s) must be modified before they can be eliminated from the body.

This is accomplished through a process that was once referred to as *detoxification*, or *drug metabolism*. However, because of the confusion over whether physicians were discussing the metabolic processes in the body or the process of breaking down a foreign chemical, the term *biotransformation* has gradually been gaining favor as the proper term when a pharmaceutical agent is being discussed, while the older term “metabolism” is often applied to illicit drugs and alcohol. They both reflect the same process, which is labeled one way if it is a prescribed pharmaceutical and the other if it is an illicit drug. Biotransformation/detoxification is usually carried out in the liver, although on occasion other tissue(s) might also be involved. The liver's *microsomal endoplasmic reticulum* produces a number of enzymes¹⁰ that transform toxic molecules into forms that might be eliminated from the body. There are essentially two forms of biotransformation: (a) the **zero-order biotransformation** process, and (b) the **first-order biotransformation** process. In the zero-order biotransformation process, the biotransformation mechanisms quickly become saturated, and only a set amount of a

⁶Discussed in Chapter 6.

⁷The most common of which is *albumin*. Sometimes, compounds are referred to as albumin-bound, rather than protein-bound. Technically, drugs that are more acidic tend to bind to albumin, while drug molecules that are more basic tend to bind to the alpha1-acid glycoprotein molecules in the blood.

⁸See Glossary.

⁹In fact, before methods of producing large quantities of penicillin were developed in the 1940s, patients' urine was collected and the penicillin was isolated, purified, and reused.

¹⁰The most common of which is the P-450 metabolic process, or the microsomal P-450 pathway.

given compound can be biotransformed each hour regardless of the concentration of that chemical in the blood (Bennett & Brown, 2003). Alcohol is an example of a compound that is generally biotransformed through a zero-order biotransformation process:¹¹ If the individual ingests alcohol more rapidly than his or her body can metabolize it, he or she will become intoxicated.

In the first-order biotransformation process, a set percentage of the compound(s) in question is biotransformed each hour, independent of the concentration of that substance in the blood. There are many compounds that are biotransformed through a first-order biotransformation process. Both the zero-order and first-order processes are carried out by the mechanisms of (Ciraulo, Shader, Greenblatt, & Creelman, 2006; Wynn et al., 2009): (1) oxidation, (2) reduction, (3) hydrolysis, and (4) conjugation. The chemistry of each form of biotransformation is quite complex, and is best reserved for those readers who wish to pick up a pharmacology textbook to review the biochemistry of the biotransformation process. It is enough for the reader to remember that there are two different forms and four different chemical mechanisms of biotransformation.

In both forms of biotransformation, the drug molecules are chemically altered as rapidly as the enzymes involved in each step can accomplish, one molecule at a time. The original substance is referred to as the *parent compound*. The goal of the biotransformation process is to alter the foreign chemical molecule until it becomes a compound that can be eliminated from the body. In some cases, depending on the chemical characteristics of the drug(s) ingested, this process might involve several steps. The intermediary molecules that emerge from this process are known as *metabolites* of the parent compound, some of which have psychoactive effects of their own. Compounds that are highly lipid-soluble require extensive biotransformation before they become less lipid-soluble and are more easily eliminated from the body, and some of these metabolites are themselves psychoactive (Jenkins, 2007; Lehne, 2013).

If the parent compound has no or minimal biological effect, and its major effects are achieved by the metabolites of that compound, then the parent compound is referred to as a **prodrug**. Most compounds in use today are biologically active, and only a small number are prodrugs (such as aspirin and codeine).

To add an element of confusion, sometimes the enzymes necessary for the biotransformation of one compound

will increase the speed of the biotransformation of a second compound, reducing its effectiveness. Also, normal variations in the individual's biological heritage or various diseases can alter the speed at which some individuals can biotransform a compound. Further, as a result of genetic variations, some individuals are able to biotransform a given compound more rapidly than are others, making them **rapid metabolizers** of that compound. Genetic variations might endow a person with a body that is slower at breaking down a given compound than is normal, making them a **slow metabolizer** of that compound. Disease states, such as alcohol-induced liver damage¹² can also alter the liver's ability to biotransform many compounds, in effect artificially making them slow metabolizers, a situation that the attending physician must also consider when prescribing a pharmaceutical to treat an ill patient. There is no way to identify these individuals other than clinical experience obtained by giving the patient a drug and observing his or her reaction, although there is ongoing research in this area.

The human digestive tract is designed not to let any chemical that is absorbed pass directly into the circulation, but to filter it first through the liver. This is called the **first-pass metabolism effect** (also known as **presystemic elimination**; DeVane, 2004, 2017). By taking chemicals absorbed from the GI tract and passing them through the liver, any toxin in that food or drug might be identified and the biotransformation process started, hopefully before the compound can do any damage to the body itself. One consequence of the first-pass metabolism process is that the effectiveness of many orally administered compounds is limited. For example, much of an orally administered dose of morphine is biotransformed by the first-pass metabolism effect before it reaches the site of action, limiting its effectiveness as an analgesic. Collectively, the first pass metabolism process, and the various subforms of biotransformation, work to prepare foreign chemicals for the last stage: *elimination*.

Elimination

So closely intertwined are the processes of biotransformation and elimination that some pharmacologists consider them to be a single topic. The process of biotransformation changes the chemical structure of a compound so that the metabolites are more water-soluble, so that it can then be removed from the circulation by the organs involved in filtering the blood. This is usually carried out by the kidneys, although the lungs, sweat glands, and biliary tract might also be involved in the process of drug elimination (Wilson, Shannon, Shields, & Stang, 2007). An example of this is the small percentage of

¹¹Technically, alcohol's biotransformation at extremely high doses does not follow the zero-order biotransformation cycle exactly, but alcohol's deviation(s) from the zero-order biotransformation cycle is best reserved for toxicology texts.

¹²Discussed in Chapter 5.

alcohol that is eliminated through the sweat and breath when the person exhales, giving the person who is intoxicated a characteristic smell.

The process of drug elimination does not happen instantly. Rather, time is required for the enzymes involved in each step of the biotransformation process to break down a specific compound. Depending on the exact compound under consideration, this process might take hours, or in the case of long-acting compounds such as methadone, days. The goal of the biotransformation process is to allow the enzymes to transform the drug molecule(s) into a water-soluble metabolite that can be eliminated from the body. This brings us to another necessary concept to consider: the drug's **half-life**.

Drug Half-Life

The concept of a drug's half-life provides a useful yardstick by which to establish the *rough* estimate of a compound's effectiveness, duration of effect, and the length of time that it will remain in the body. There are several different forms of drug half-life, depending on different aspects of the compound's actions in the body. We will discuss some of the more important of these half-life forms in this section.

Distribution half-life is the time that it takes a compound to work its way into the general circulation after it is administered (Reiman, 1997). This information is important to physicians in overdose situations, where it is necessary to anticipate the long-term effects of compounds involved. It is also of importance in planning pharmacological interventions: If a patient is in acute pain, you would want to administer a compound that was able to rapidly reach the circulation rather than a compound that is absorbed slowly. A patient in chronic pain might benefit more from a compound that is more slowly absorbed but which provides a steady level of analgesia to control their discomfort.

There are two subforms of distribution half-life (Cloos, 2010a): The **alpha half-life** is the period following peak concentration of the drug in the blood and when it is redistributed to various body tissues. The **beta half-life** is the decline in plasma concentration as the drug is biotransformed and eliminated from the body (Cloos, 2010a). This information is important for understanding the pharmacokinetics of a compound. For example, the beta half-life is often the criterion on which a benzodiazepine is classified as being a short-, intermediate-, or long-acting compound (Cloos, 2010a).

Therapeutic half-life is a rough measure of a compound's duration of effect. The therapeutic half-life is

the time necessary for the body to inactivate 50% of a compound. This may be complicated by compounds whose metabolites also have a biological effect on the body. The therapeutic half-life usually is a reference to a single dose of a compound, and regular dosing of that compound can alter the therapeutic half-life of a chemical. Finally, there is the **elimination half-life** of a compound. This is the time that the body requires to eliminate 50% of a compound. Again, the elimination half-life is usually a reference to the time that it takes for 50% of a single dose of a compound to be eliminated from the body. In medical practice, it is usually assumed that after the fourth or fifth dose, the individual will have achieved a *steady state* of a compound in his or her blood. Two factors that influence the elimination half-life are the individual's liver and kidney functions. The elimination half-life of a compound might be extended in persons with impaired liver or kidney function, and the physician must make dosage adjustments for persons with such problems.

The various half-lives of a compound are not the same. A compound might have a therapeutic half-life of minutes but an elimination half-life of hours, as is demonstrated by several of the ultra-short-acting barbiturates.¹³ Further, all half-life estimates are based on the assumption that the patient has only used one compound. If the patient is using multiple compounds, it becomes more difficult to estimate the drug half-lives, since multiple drugs would then compete for the processes of absorption, distribution, biotransformation, and elimination.

One popular misconception is that it only takes two elimination half-life periods to remove a compound from the body. In reality, fully 25% of the initial dose remains after the end of the second half-life period, and 12% of the dose is still in the body after three half-life periods. Pharmacologists estimate that it will take five half-life periods before all of a single dose of a chemical is eliminated from the user's body, thus completely undoing the steady state mentioned above.

DRUG INTERACTIONS

In cases where a patient is receiving multiple medications, there is a very real danger of these compounds interacting in ways not anticipated by the individual. Wynn, Oesterheld, Cozza, and Armstrong (2009) estimated that 5% of all hospitalizations in the United States were the result of adverse drug–drug interactions, with uncounted numerous less severe interactions causing the patient distress but not requiring hospitalization. Serious drug–drug interactions result in

¹³Discussed in Chapter 6.

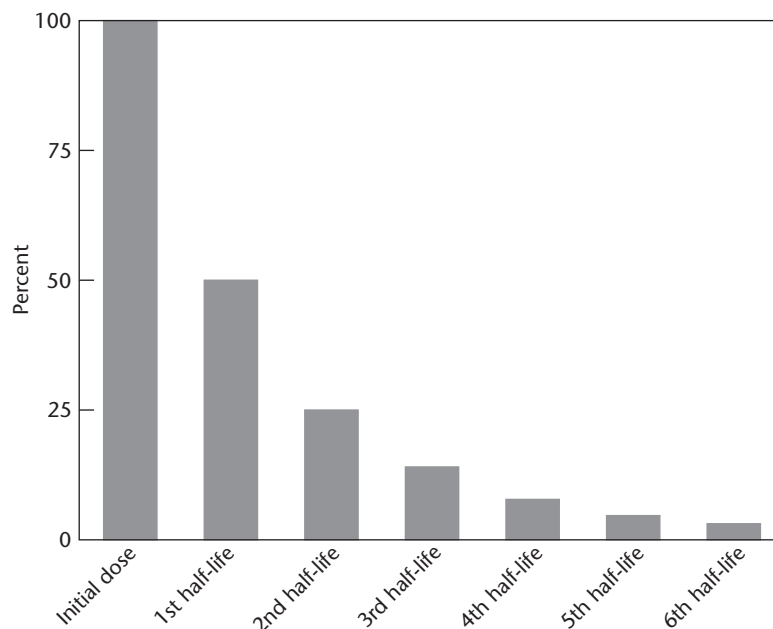


FIGURE 3-2 Drug Elimination in Half-Life Stages.

an estimated 7,000 deaths in this country alone, although this is only an estimate, as many such fatal interactions probably are not reported, or the deaths are attributed to other conditions, according to the authors.

The Effective Dose

The concept of the **effective dose** (ED) is based on dose-response calculations in which scientists have calculated the approximate dose at which a given percentage of the population will respond to a given dose of a compound. For example, the dose at which 10% of the general population is expected to have the desired response would be identified as the ED_{10} , while the dose at which 50% of the general population is expected to have the desired response would be identified as the ED_{50} . Obviously, if you were a biochemist developing a new compound, you would want to find a dose level allowing as large a percentage of the general population as possible to achieve the desired response. It would appear at this point that you could simply keep increasing the dose until *everybody* responded to the new drug. However, as dosage level increases, you (a) encounter the **ceiling dose effect** and (b) risk development of toxic reactions. The ceiling dose effect is just that: a dose above which additional drug molecules will not have any additional effect. Acetaminophen and ibuprofen are good examples of such compounds (discussed in Chapter 16). If an individual were to ingest

more than the ceiling dose, s/he would only be more likely to experience a toxic reaction.

The Lethal Dose and Therapeutic Index

This brings us to another useful concept: the *lethal dose*. Drugs are, by definition, foreign to the body, and while they might disrupt a body function(s) in a specific manner, they also present the risk of altering that body function so much that the user dies. A hypothetical compound that suppressed respiration at a certain dose might be a useful pharmaceutical for certain forms of surgery. However, too large a dose would run the risk of the individual's respiration being suppressed permanently—hardly a desired response!

During the era in which the atomic bomb was being developed, scientists calculated the amount of radiation a person might be exposed to without becoming terminally ill. Such dose-response curves estimate what percentage of the population would die as a result of being exposed to a certain dose of radiation, a chemical, or a toxin. This figure is then expressed as the *lethal dose (LD) ratio*. A dose of a drug that would cause 1% of the population to die would be abbreviated as the LD_{01} , and the dose that in theory would kill 25% of the population would be abbreviated as the LD_{25} , etc. For example, 1% of patients with a blood alcohol concentration of 0.350 mg/mL would be expected

to die without medical help. Thus, for alcohol, the LD_{01} would be 0.350 mg/mL of blood.

By comparing the effective dose and lethal dose ratios, it is possible to obtain a raw estimate of the **therapeutic window** or the *therapeutic index* of a compound. If you had a hypothetical chemotherapy compound used to treat cancer that had an ED_{99} of 100 mg, and an LD_{001} (meaning only 1 death per 1000 patients receiving this dose), that compound would be said to have a wide therapeutic window. If in contrast this same hypothetical compound had an ED_{99} at 100 mg but had a LD_{30} , it would be said to have a narrow therapeutic window. Unfortunately, many of the drugs that are misused have very narrow “therapeutic” windows, the result being that it is very easy to overdose on these compounds.

Therapeutic Threshold and Peak Effects

As drug absorption progresses following a single dose of a compound, the amount of a compound in the individual's circulation will increase until it reaches the minimal level at which that compound might be effective. This is the **therapeutic threshold** for that compound. As blood level rises over time, the effects will continue to become stronger and stronger until the drug reaches its *peak effect dose*. Then, as the process of biotransformation proceeds, the effects of the compound will diminish until the blood levels of the compound fall below the therapeutic threshold.

The period of peak effects varies from one compound to another. For example, the peak effects of one of the ultra-short-acting barbiturates might be achieved in a matter of seconds after the compound is injected into a vein, while a long-term barbiturate might take hours to achieve its peak effects. Further, variables that affect absorption, distribution, biotransformation, and elimination will also have an impact on when a given compound reaches its peak effects.

The Site of Action

Essentially, the **site of action** is where the compound(s) carry out their main effects. For most of the psychoactive pharmaceuticals, and the various drugs that are misused, various neurons in the central nervous system (CNS)¹⁴

will be the site of action. The CNS is, without question, the most complex organ system found in the human body. At its most fundamental level, the CNS is comprised of approximately 100 billion neurons, each of which receives input from tens, hundreds, or perhaps thousands of other neurons. This is accomplished through molecular neurotransmitters that are released by one neuron¹⁵ with the goal of activating a receptor site on the next neuron in that neural chain.¹⁶

Although much of the CNS is squeezed into the confines of the skull, the individual neurons usually do not actually touch. Rather, they are separated by microscopic spaces called **synapses**. To communicate across the synaptic void, or synaptic gap, one neuron will release a cloud of chemical molecules that function as *neurotransmitters*. To date, more than 50 compounds have been identified that function as neurotransmitters within the brain (Drazinic, Szabo, Gould, & Manji, 2017), but the greater percentage of these neurotransmitters will remain outside of the scope of this text.¹⁷ The role that neurotransmitters play in the process of information transfer between neurons will be discussed later in this chapter.

The Receptor Site

At its most simplistic, the receptor site is the location on neuron “B” that receives information “A.” This is accomplished through the process of neurotransmission. To understand the concept of a receptor, imagine the analogy of a key and a lock. The receptor site, by way of analogy, can be viewed as a lock, although on a molecular scale, and is usually a protein molecule located in the cell wall of the neuron. In normal neurotransmission, the molecular “key” (neurotransmitter molecule) slides into the “lock” (receptor site). Not every receptor site is located in the CNS: Certain specialized neurons will leave the central nervous system to transmit messages from the brain to specific organs in the body (muscle cells, for example). A point that must be clarified is that we have discussed receptor sites in the singular to help make the whole process of neurotransmission easier to understand. This is a gross simplification, as a neuron might have hundreds or even thousands of receptor sites for a variety of compounds, some of which function as neurotransmitters. As interesting as the study of receptor sites might be, and this actually is an interesting topic, we must move on to the process of neurotransmission.

¹⁴Although the CNS is by itself worthy of a lifetime of study, for the purposes of this text the beauty and complexities of the CNS must be compressed into a few short paragraphs. Those who wish to learn more about the CNS are advised to seek a good neuroanatomy, neuropsychology, or neurology textbook.

¹⁵Called the “upstream” neuron.

¹⁶Called the “downstream” or “postsynaptic” neuron.

¹⁷I bet you thought that I was going to name them all, didn't you?

The Process of Neurotransmission¹⁸

If you were to examine a properly prepared section of the human brain under a powerful microscope, you would discover that the neurons do not quite touch each other but are separated by small gaps called **synapses**, or **synaptic junctions**. Each individual neuron might have dozens, hundreds, or thousands of such junctions, and if you were to count each one individually you would discover that the total number of synaptic junctions is larger than the total number of grains of sand on all the beaches on Earth combined (Stahl, 2008).¹⁹ Yet each neuron is isolated from its fellows by the synaptic junctions that have developed over the years, which would appear to make the process of information processing virtually impossible.

Neurotransmitters

Nature's solution to this apparent conundrum is to have one neuron²⁰ release a microscopic burst of chemical messengers that will cross the synaptic gap and bind at a receptor site in the wall of the next neuron²¹ (Bennett & Brown, 2003; Olson, 2006). That chemical messenger is the neurotransmitter. Some of the neurotransmitters that are relevant to this text include histamine, insulin, the subtypes of dopamine, the subtypes of serotonin, norepinephrine, acetylcholine, glutamate, and gamma-aminobutyric acid²² (GABA).

The strength of the attraction of the neurotransmitter molecule for the receptor site is called the *affinity* of that molecule to the receptor. Obviously, the neurotransmitter molecules have a high affinity for their intended receptor site. However, on occasion, a compound might also have a lower affinity level for an unintended receptor. This is seen most often with man-made chemicals and is one reason why a compound might induce side effects, discussed earlier in this chapter. To avoid the spurious generation of a message that will be passed from one neuron to the next, a specific number of receptor sites on the postsynaptic neuron must be occupied by the appropriate neurotransmitter at the same instant. This can only be achieved if the presynaptic neuron released sufficient numbers of the appropriate neurotransmitter

molecules at once to achieve the critical level necessary for neurotransmission to take place. When this critical level is reached, a profound change is triggered in the postsynaptic neuron, and an electrochemical message flashes through the downstream neuron either causing it to "fire" (pass the message on to the next neuron by releasing its stores of neurotransmitter molecules to the next neuron in the network²³) or inhibit the firing of the downstream neuron. In the human brain, the main excitatory neurotransmitters that are of importance in substance misuse are glutamate and aspartate, while the main inhibitory neurotransmitter is GABA.

The response of the postsynaptic neuron falls into one of two categories: The *fast* or *ionotropic response*, which usually involves the downstream neuron altering the speed with which it can fire and pass the message on to the next neuron in that neural network. The presynaptic neurotransmitter molecules might also initiate a *metabotropic response*, involving long-term alterations in the post-synaptic neuron. These include (Stahl, 2008): making or destroying synaptic junctions, reinforcing neural networks, urging axons to sprout, the synthesis of proteins and enzymes, and neurotransmitter receptors that regulate the function of the postsynaptic neuron.

Neurotransmitter Reuptake/ Destruction

Once the neurotransmitter molecules have been released and carried out their function at the receptor site, one of three things can happen to those neurotransmitter molecules: (a) They can be retrieved by the upstream neuron through the use of molecular reuptake pumps, (b) they can be destroyed by enzymes near the receptor sites produced by either the presynaptic or postsynaptic neuron, or (c) they can diffuse into the surrounding area and eventually be removed.

Co-Transmission

When neurotransmitters were first discovered, scientists believed that each neuron released just one neurotransmitter type. However, it has since been discovered that neurons both transmit and receive *secondary neurotransmitter* molecules, which often have far different characteristics than those of the primary neurotransmitter. The process of releasing both types of neurotransmitters is called *co-transmission*. To illustrate this process, imagine a neuron that releases serotonin as the primary neurotransmitter. It

¹⁸ Admittedly, this is a very simplified summary of the neurotransmission cascade, but it should be sufficient for the purposes of this text. There are a number of very good books on neuroanatomy that provide a detailed description of this process, if you should wish to pursue this area for further study.

¹⁹ Or the total number of stars in the universe.

²⁰ Called the "upstream" neuron.

²¹ Called the "downstream" or postsynaptic neuron.

²² Which binds at the N-methyl-D-aspartate (NMDA) receptor site.

²³ In the process of which the neuron is transformed into the upstream neuron for the third neuron, etc., etc., etc.

might also release small amounts of norepinephrine during the process of neurotransmission. The norepinephrine molecules might indicate to the upstream neuron that sufficient amounts of serotonin have been released (sort of a chemical “cease-fire” message), or trigger the activation of molecular reuptake pumps to retrieve as many serotonin molecules as possible for reuse.

Tolerance

Tolerance to a compound is defined as “a shortened duration and decreased intensity of drug effects after repeated administration” (Ghoneim, 2004b, p. 1279). When the compound is a mood-altering substance, this process is also known as **neuroadaptation**, especially if the compound was prescribed by a physician. Unfortunately, many people still use the older term of “tolerance” for both prescribed and illicit use of a compound. Clinicians now use the word neuroadaptation for situations where a compound has a shortened duration of effect because the brain has learned to compensate for the presence of the compound. At a behavioral level, the individual misusing a substance might admit that it takes more of his or her drug of choice to achieve a desired level of intoxication than in the past. There are many mechanisms through which tolerance develops, including:

Metabolic tolerance: Through this process, the body becomes more proficient in the process of biotransformation of certain compounds, at least for a limited period. This is commonly seen in the early stages for some AUDs, for example, where the individual will report that s/he must use more alcohol to achieve the same level of intoxication once achieved with a lower level of alcohol intake (Nelson, 2000). Unfortunately, the liver can only maintain this extra effort at alcohol biotransformation for a limited period before it starts to break down, resulting in the phenomenon of lower tolerance to alcohol often found later in the individual’s life.

Behavioral tolerance reflects the behavioral outcome of the brain’s efforts to maintain normal function in spite of the presence of foreign molecules. The individual’s behavior appears almost normal, in spite of the presence of a psychoactive compound in their body. Again, using alcohol as an example, even law enforcement or health care professionals are shocked to discover that an individual who appeared to be mildly intoxicated is in reality significantly over the legal blood alcohol level. The behavior did not reflect the individual’s true blood alcohol level.

Cross-tolerance: Multiple compounds might affect the body through similar mechanisms, such as when two

or more compounds possess some affinity for the same receptor site. In this case, the receptor site in question would react to the presence of either compound. As the neuron adapts to the constant presence of the first compound, these cellular changes (usually at the level of receptor sites) also influence the neuron’s ability to react to the presence of molecules from the second compound. Alcohol and the benzodiazepines provide a good example of this process: As the neuron adapts to the continual presence of alcohol by up-regulation of receptor sites, it will become less sensitive to the benzodiazepines, which use the same GABA receptors to achieve their effects.

Reverse Tolerance, or what is also called **sensitization**, is a poorly understood phenomenon in which lower doses of a compound produce the same effect as higher doses did when the use of the substance was initiated (O’Brien, 2011). There is a possibility that the process of operant conditioning contributes to the individual’s expectations of the compound’s effects, making him or her more responsive to lower doses than were originally used (O’Brien, 2011).

Up-/Down-Regulation of Receptor Sites

The individual neurons attempt to maintain a relatively stable level of function. The molecules of any neuroactive compound, including drugs that are misused, alter the normal function of the various neural networks, the individual members of which attempt to counteract the influence of that compound (Breggin, 2008; Cruz, Bajo, Schweitzer, & Roberto, 2008). One mechanism through which individual neurons attempt to maintain stable levels of activation is either the **up-regulation**²⁴ or **down-regulation**²⁵ of the number of receptor sites. If the neuron is constantly being subjected to high levels of a neurotransmitter, it might down-regulate (which is to say, reduce) the number of receptor sites so that the neurotransmitter molecules have fewer “targets.” Some of the neurotransmitter receptor sites would be absorbed back into the neuron. However, if the neuron was not being exposed to high levels of the neurotransmitter, it might increase (up-regulate) the number of receptor sites, making it easier for the neurotransmitter molecules to find a receptor site.

Drug Agonists/Antagonists

Essentially, a drug **agonist** is a compound that activates a receptor site by being able to mimic or enhance the actions of

²⁴See Glossary.

²⁵See Glossary.

a natural neurotransmitter (Wilson et al., 2007). For drugs that are misused, the receptor sites are the individual neurons of the brain (as well as elsewhere in the body), and the more closely the molecule resembles a naturally occurring neurotransmitter, or the greater the affinity of that molecule for that receptor site, the stronger the drug's effect will be on the neuron. The analogy of a skeleton key for a lock would not be out of place here: The narcotic analgesic family of compounds use binding sites in the brain's pain perception system; however, the narcotics are not perfect matches for these receptor sites and only simulate the effects of naturally produced opioid-like molecules far less efficiently than their endogenous cousins.

However, some compounds are able to fit into the receptor site *without* activating it. Such compounds are called **antagonists** (or antagonists). The drug Narcan (used to treat narcotic overdoses) functions as an opioid antagonist, blocking the opioid receptor sites without activating them, thus preventing the narcotic molecules from reaching the receptor sites in the brain. The analogy of a key that was broken off just beyond the handle might not be out of place here. There are also compounds that are *partial agonists*. This means that the drug molecules are able to activate the receptor site very weakly, if at all, while preventing other drug molecules from binding at that receptor site. Again, using the lock-and-key analogy, imagine the night watchman who has a ring full of keys and is forced to go through key after key to find the right one for a specific lock. Some of the keys might match some of the tumblers in the lock, but only one will match the specific combination necessary to open that lock.

Potency

The potency of a biologically active compound is the ratio between the size of a dose and the desired response (Ghoneim, 2004b). The difference between the effective dose of heroin and morphine illustrates this point. The standard conversion formula is that 4 milligrams of pharmaceutical-quality heroin²⁶ provides the same degree of analgesia as 10 milligrams of morphine. Thus, heroin is said to be more potent than morphine. The pharmacology of both compounds will be discussed in Chapter 11.

The Blood-Brain Barrier

The human brain is an energy-intensive organ, receiving ten times as much oxygen and nutrients as any other organ in the body. Twenty percent of the blood pumped with each

heart beat is sent to the brain to supply it with needed nutrients and oxygen. However, the brain is also an especially vulnerable organ, and direct contact with blood is toxic to neural tissue. To protect the brain from direct exposure to blood while still allowing necessary nutrients to reach neural tissues, nature has provided the brain with a circulatory system in which endothelial cells are tightly joined around the capillaries (Interlandi, 2013). The closely packed endothelial cells are part of the **blood-brain barrier**²⁷ (or BBB), which is composed of the endothelial cells and a thin layer of cells known as **astrocytes**²⁸ or **pericytes**, which collectively separate the brain from direct contact with the circulatory system.

Although it is referred to as a "barrier," the BBB is better thought of as a selective screen. However, if it is intact, the BBB will protect the brain from invasion from a range of microorganisms and toxins. There are specialized cellular transport mechanisms between or within the endothelial cell walls, each one adapted to allowing one type of water-soluble molecule such as glucose, iron, and certain vitamins to pass through the BBB into the neural tissues. Lipids are also able to pass through the endothelial cells, by first binding with and slowly passing through the cell walls of the endothelial cells to eventually reach the brain. In the process, most compounds that are lipid-soluble are also admitted into the brain. Although it is an imperfect system, the BBB does an exceptional job of protecting the brain from toxins or microorganisms that would otherwise destroy it.

Chapter Summary

The field of pharmacology, and the subspecialty of neuropharmacology, are each worthy of a lifetime of study. It is not possible to do justice to either topic in this text. However, an understanding of some of the basic pharmacology concepts is necessary to better understand how drugs that are misused are administered, absorbed, distributed, and biotransformed/eliminated from the body. The concepts of the drug agonist, the antagonist (or antagonist), and the mixed agonist/antagonist were introduced. A brief overview of the blood-brain barrier, and its function was provided, and the concepts of tolerance and cross-tolerance to a compound were reviewed.

²⁶Heroin is an accepted pharmaceutical in many countries. Obviously, we are talking of pharmaceutical-quality heroin, produced in facilities that meet the regulations of the appropriate regulatory agencies, and not the illicit heroin sold on the streets of the United States.

²⁷To learn more about the blood-brain barrier, please review this subject in a good biological psychology or neurology textbook.

²⁸See Glossary.

An Introduction to Alcohol: Man's Oldest Recreational Chemical

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 4.1 Understand the history of alcohol
- 4.2 Understand the use of alcohol in present times
- 4.3 Identify the scope of alcohol use in the United States today
- 4.4 Describe the pharmacology, including subjective effects, of social use of alcohol
- 4.5 Comprehend the medical complications of social use of alcohol

... humans, as a species, like to drink. We consume wine, beer, cider, spirits ... in fact the fermented product of almost anything we can turn to alcohol

—Dunn (2013, p. 38)

Introduction

Ethyl alcohol¹ is occasionally found in the natural world, especially in various forms of fruit that ripen at specific times of the year. Various animal and insect species have learned to identify these fermented fruits by smell, in many cases apparently enjoying the effects of the alcohol produced by the process of fermentation (Dunn, 2013). Our ancestors, who were quite familiar with the world around them, might have rushed to join these animals, although this is based only on historical speculation. By the time modern society emerged, they knew which fruits and tubers would ferment at certain times of the year to provide a naturally occurring cocktail or two (Tucker, 2011).

Arguably, the development of fixed settlements and the rise of agriculture could be traced at least in part to the discovery that the surplus crops being cultivated could be allowed to ferment as a way of preserving them for use as a beverage. A liquid beverage is easier to store than grain and is less likely to spoil. Unbeknownst to those early farmers, the yeast involved in the fermentation

¹The designation *ethyl* alcohol is important to chemists, as there are at least 45 other compounds that might be classified as form of alcohol. Each of the other forms of alcohol is toxic to the body, although the length of time that is necessary for the toxic effects to manifest varies from compound to compound (Keany, 2011). *Ethyl alcohol* is the one most commonly consumed by humans, and these other forms of alcohol will not be discussed further.

process might even have contributed to the nutritional value of the beverage by adding various vitamins and amino acids to the mixture (Dunn, 2013). One could argue that “civilization”² itself could be traced to the need for semi-permanent or permanent communities to house these early farmers (Dunn, 2013). Alcohol has continued to play a role in lubricating social interactions throughout history, and, given its role in society today, it is important for the reader to have a working understanding of alcohol, how it is obtained, and the effects of social alcohol use.

Why Do People Consume Alcohol?

Theoretically, alcohol is but one of a rather extensive range of naturally occurring compounds ingested by humans for their psychoactive effects (McGovern, 2009). Mushrooms containing compounds with hallucinogenic potential are found in some parts of the world, but alcohol use is ubiquitous. Scientists exploring the ruins of various cities in what was once the ancient Sumerian empire have found numerous clay tablets devoted to the process of brewing beer, especially a form of beer made from fermented honey known as mead (Cahill, 1998). Early alcohol-containing drinks (a) supplied at least some of the fluids necessary for the individual’s daily survival, (b) were a valuable source of energy,³ (c) and had mild antibacterial properties that often made them safer to ingest than the local water⁴ (Johnson, 2006; Millman, 2013).

Currently, individuals consume alcohol for a variety of reasons: In limited quantities, it has some health benefits, and when used for short periods of time functions as a **hypnotic**,⁵ alcohol induces a sense of well-being or in some cases euphoria in the individual, feelings that have added to the allure of alcohol throughout history. Alcohol can also facilitate social interactions, some of which, unfortunately, have led to countless thousands of unplanned children over the years (Dunn, 2013). It is used in certain religious rituals, and, on very rare occasions, by physicians for medicinal purposes. Folk medicine holds that a teaspoon of brandy helps to break up mucus in the lungs, allowing the congested individual to breathe more easily. While this theory is attractive, it is for its ability to induce a sense of well-being and euphoria that most

people consume alcohol even if it is done under the pretense of being “my cough medicine.”

Daily consumption of *one* glass of wine a day appears to lower an individual’s risk of developing cancer of the esophagus by about half, compared to those who do not drink (Kubo et al., 2009). Unfortunately, this effect is found only for wine, suggesting that it is perhaps a compound in the wine and not the alcohol itself that reduces the individual’s risk for this form of cancer. As will be discussed in the next chapter, *heavy* alcohol use is a risk factor for the development of cancer of the esophagus, making the use of alcohol to avoid this form of cancer a dangerous practice (Kubo et al., 2009).

A Brief History of Alcohol

There is strong evidence that some insects and many animals are attuned to the smell of fruit and are drawn to it, a trait that early naturalists capitalized upon to capture specimens (McGovern, 2009). Since seed pods, which are the fruit that we consume, are also usually quite visually striking, animal species that use visual cues to obtain food will be drawn to these fruit pods. Some plants capitalize on the affinity of insects for them as a means of pollination, while animals that ingest the seed pods play a role in the distribution of that species by spreading seeds across their respective territories (thoughtfully, complete with a little packet of fertilizer).

However, from time to time the outer skin of the fruit will crack or break open, allowing microorganisms entry to the lush interior of the fruit pod. In some of the fruit pods the process of fermentation will begin as yeast settles on the fruit and begins to consume it. From the perspective of the yeast, ethyl alcohol is not the goal of fermentation but only a waste product. In spite of its status as waste from the process of fermentation, alcohol is a concentrated source of energy. This, plus the intoxicating effects of alcohol, apparently served as incentives for many animal species to seek out and consume it if it was available. Researchers have observed tree shrews selectively sipping nectar from certain palm flower clusters in which the process of fermentation has taken place (“A tree shrew’s favorite tippie,” 2008; McGovern, 2009). The liquid found in these palm flower clusters after fermentation has an alcohol content of 3.8%, approximately the same as modern beer. It is not unreasonable to assume that ancient hominids shared this preference for alcohol when it could be obtained.⁶

²Are we “civilized”? This is an arguable point.

³One end product of alcohol metabolism is glucose, a blood sugar.

⁴From a reproductive perspective, it is more advantageous for the individual to die from cirrhosis of the liver in his or her 40s than from a water-borne disease when the person is a child or adolescent (Johnson, 2006; Millman, 2013).

⁵See Glossary.

⁶This is only a theory as there is little evidence of intoxicated hominids in the geological strata in which these fossils are found. A *Homo habilis* skeleton from an intoxicated member of that species, when found by anthropologists, would look the same as any member of *Homo habilis*, although one might argue that their intoxication might have contributed to their opportunity to become fossilized if it made them ignore predators in the area.

Mead, a form of beer made from fermented honey, appears to have been in widespread use during the latter part of the Paleolithic Era,⁷ while beer made from other ingredients might date back to 9000 B.C.E. (Heilig & Spanagel, 2015; Millman, 2013; Tucker, 2011). Although controversial, some claim preliminary evidence shows that a form of beer was being manufactured in Upper Egypt 18,000 years ago (Tucker, 2011). Beer was considered part of a worker's pay: The workers who constructed the pyramids in Egypt received a daily ration of 4 liters of beer (Millman, 2013). These early forms of beer were quite thick and nutritious. By comparison, modern forms of beer are rather thin and anemic, contributing little to the individual's dietary needs. Historically, the use of beer and wine as dietary agents are reflected in the fact that both are mentioned in Homer's epic poems the *Iliad* and the *Odyssey*.

The earliest written record of wine making is found in an Egyptian tomb that dates back to 6,000 years ago (Heilig & Spanagel, 2015). By the time of the Greek and Roman empires, wine was a central part of civilized life, in part because of its nutritional value (Walton, 2002). Alcohol is an extraordinary source of energy,⁸ providing as much energy as can be obtained from fat, and far more energy than from carbohydrates and proteins (Lieber, 1998). Ancient Greek prayers for slain warriors expressed the hope that they would enjoy a state of continuous intoxication in the afterlife. In pre-Christian Rome, intoxication was seen as a religious experience⁹ (McGovern, 2009; Walton, 2002). The Bible refers to alcohol as nothing less than a gift from God, and during the Middle Ages monks in various abbeys experimented with methods of wine production and discovered how to produce champagne (Woods, 2005) and various liquors. As early as the 8th century B.C.E. alchemists working in what is now modern Iraq had started to experiment with the process of distillation, allowing for the development of more concentrated alcoholic beverages (Blum, 2010; Tucker, 2011).

Beer and wine consumption continued through the Renaissance in Europe, the Age of Exploration, and into the early colonial period when the first colonies in the

New World were established.¹⁰ In England, the Quakers started to emphasize chocolate as an alternative to drinking alcohol, establishing the foundation for the chocolate industry in England (de Lange, 2015). Alcohol use was ubiquitous in the colonies and the early United States,¹¹ and the imposition of a federal tax on liquor to help repay loans from the French to help fund the Revolution led to the famous Whiskey Rebellion in the United States (Okrent, 2010). This tax was discontinued in 1802, but was resurrected to help pay for the War of 1812, and was again allowed to expire in 1817. In 1862, a liquor tax was enacted yet a third time to help pay for the Civil War, after which time the government found itself permanently dependent on the excise tax to help pay for its operating expenses (Okrent, 2010).

Alcohol use has been a contentious issue in Western society. By the start of the 19th century, public intoxication was viewed not as a sign of religious ecstasy but as a public disgrace. In many communities during the latter part of the 19th and early 20th centuries, it was not uncommon for poorer people to "sell" their vote for credit slips at local bars (Okrent, 2010). In some communities in the United States there was a licensed drinking establishment for every 100 citizens, including women and children.¹² Widely disparate groups found common ground in opposing the sale and use of alcohol in the United States, and two years after the end of World War I this country embarked on a social experiment known as Prohibition. During this period, alcohol use was, in theory, prohibited except when a physician prescribed it for the treatment of disease. Use of alcohol was at times openly flaunted, even when the law was still in effect.¹³ The law was repealed after approximately 13 years.¹⁴

¹⁰When the Puritans set sail for the New World, for example, they stocked their ship with 14 tons of water, 10,000 gallons of wine, and 42 tons of beer (McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds, 2009). Historians have suggested that the main reason they elected to settle in Plymouth was that they had exhausted their supply of beer on the voyage across the Atlantic and needed to grow crops with which to produce more (McAnnalley, 1996).

¹¹A little-known fact is that John Chapman ("Johnny Appleseed") spread seeds that produced apples that tasted horrible, but which were ideal for fermenting into "hard" apple cider, which is to say apple cider containing alcohol (Okrent, 2010).

¹²There were also an unknown number of *unlicensed* drinking establishments in each community, although since by definition they were not licensed, the exact number remains unclear.

¹³To replace the tax monies lost with the onset of Prohibition, when the exercise tax on alcohol ceased to exist, Prohibitionists suggested that another form of taxation be reinstituted: the income tax (Okrent, 2010).

¹⁴Prohibition started in 1920 and ended in 1933.

⁷During what is commonly called the Late Stone Age.

⁸It has been estimated that the average adult in the United States obtains 99 calories a day from alcoholic beverages (Nielson, Kit, Fakhouri, & Ogden, 2012). However, this is an average, with individuals who do not drink obviously obtaining zero calories from alcohol, while individuals who are more studious in relation to drinking will obtain more than 99 calories/day from alcohol.

⁹For example, a Roman proverb suggested that "Bathing, wine, and Venus exhaust the body; that is what life is about."

Alcohol Today

In the time since the process of distillation was developed, various fermented beverages made with a wide variety of flavors and in different concentrations of alcohol¹⁵ have been developed. In the United States, beer is the most common form of alcoholic beverage sold, and it has an alcohol content of 3.5 to 5%, although some specialty beers have an alcohol content of less than 3% or greater than 9% (Devour, 1999; World Health Organization, 2014). It has been estimated that 6.4 billion gallons of beer are consumed each year in the United States, although there is significant interstate variation (Kirin Company, 2016).

Wine made in the United States is usually made from the fermentation of grapes, or, less often, other fruits. In other countries, other substances are often used in the process of fermentation, such as the famous rice wine of Japan known as *sake*. In the United States, wine usually has an alcohol content of between 8 and 17%, although light wines might have as little as 7% alcohol, and wine “coolers” only 5–7% by weight (Devour, 1999). The process of distillation allows for some distilled spirits to be added back to wine, to form a beverage with a higher content. These are the “fortified” wines, which may have an alcohol content as high as 20–24% (Devour, 1999). “Hard” liquors usually contain 30–50% alcohol by volume, although in some cases the alcohol content might be as high as 80% or more (Devour, 1999). While high levels of alcohol ingestion can result in a sense of intoxication, scientists are attempting to identify ways in which this might be avoided, or ways in which the individual might recover from intoxication more rapidly (Motluk, 2006).

How Alcoholic Beverages Are Produced Today

The production of wine had become relatively standardized in Europe and the Middle East by the time of the Greek and Roman empires. It was not until around the year A.D. 800, however, that an Arab chemist experimented by boiling wine and collecting the steam that was produced by this process. Since alcohol boils at about 172°F while water boils at 212°F, it is possible to heat a container of wine to the boiling point of alcohol but before it reaches the boiling point of water and collect the steam, which will contain a higher concentration

¹⁵A standard by which alcoholic beverages are measured is that the drink must contain 12 grams of ethanol. This is the amount of alcohol found in one standard 12-ounce can of beer, 1.5 ounces of an 80-proof liquor, or 4 ounces of regular wine.

of alcohol than the original wine. A cap placed over the container in which the wine is heated then directs the vapors to a metal coil that allows them to cool and form a liquid with a higher alcohol concentration than the original wine.¹⁶ This is the process of **distillation**, which historical evidence suggests had reached Europe by around A.D. 1100 (el-Guebaly, 2008; Walton, 2002). Shortly afterward, wine makers in Italy started using distillation to obtain these concentrated “spirits.”

Over the years, they learned to mix these spirits with various herbs and spices to produce different flavored beverages. Physicians were quick to seize on the new beverages as a possible medicine in an era when little was known about disease or its treatment. Consumers were quick to recognize that the resulting drink was more potent than the original wine, allowing the individual to more quickly achieve a state of intoxication. An additional advantage was that distilled spirits did not spoil as rapidly as did wine. For these reasons, distilled alcohol soon gained popularity for both medicinal and recreational use.¹⁷

Unfortunately, during the process of distillation, many of the amino acids and vitamins found in the original wine are lost. Thus, while they are a rapid source of intoxication, the concentrated alcohol that results from the process of distillation is nutritionally empty. Reliance on this nutritionally neutral beverage can, if consumed to excess often enough, contribute to the condition known as avitaminosis, which will be discussed in the next chapter. However, alcohol is prized for its ability to produce a state of relaxation and a state of altered consciousness, which at its extreme is called *intoxication*. In a very real sense we have come full circle, producing at will the same fluid so prized by insects and animals in the wild so that we might share the joys of intoxication with them.

A Working Definition of Social Drinking

It is difficult to define “social” drinking, in part because most research studies rely on retrospective analysis of the frequency of alcohol use and the amount consumed, each of which is subject to distortion (Lezak, Howieson, Bingler, &

¹⁶The alcohol concentration is measured in “proof” units. There are several competing theories about the origin of the term, which will not be discussed further here. The conversion formula is that a 10% alcohol concentration is 20 “proof” units, or a 1:2 ratio.

¹⁷A little-known fact is that, after leaving the White House after his second term in office ended, George Washington went into the distillation business and was able to produce up to 11,000 gallons of whiskey per year on his plantation, much of which was sold for profit (Zax, 2008).

Tranel, 2012). *Social drinking* is often defined as *no more than* two standard “shots” (1.5 ounces each) of liquor, two standard (12-ounce) servings of beer, or two standard glasses of wine in a 24-hour period (Lezak et al., 2012). This is somewhat consistent with the U.S. Department of Health and Human Services and U.S. Department of Agriculture’s (2015) definition of *moderate drinking*, although the guideline is more specific in that it limits the intake of alcohol to one standard serving per day for women. *Alcohol misuse* goes beyond social drinking, and would encompass *high-risk drinking* (including such things as drinking while pregnant or drinking prior to the legal age) and *excessive drinking* (which includes *binge drinking* and *heavy drinking*) (U.S. Department of Health and Human Services & U.S. Department of Agriculture, 2015). Thus, alcohol use disorders would surface within the broader category of alcohol misuse. A *binge* is defined by some as when a man consumes five or more standard drinks, glasses of wine, or standard servings of beer in a 2-hour period, or when a woman consumes four or more standard drinks, glasses of wine, or servings of beer in a 2-hour period (U.S. Department of Health and Human Services & U.S. Department of Agriculture, 2015), whereas the National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2004) adds the specifier to this definition that the blood alcohol concentration (BAC) is brought up to 0.08. Heavy drinking is defined as 8 or 15 (women vs. men) drinks per week (U.S. Department of Health and Human Services & U.S. Department of Agriculture, 2015), whereas *low-risk drinking* has been defined by the NIAAA as four drinks in one day up to 14 drinks in a given week for men, compared to three drinks in one day up to seven in a given week for women. Those within this last guideline are at low risk of developing an alcohol use disorder.

The person with an alcohol use disorder (AUD) will experience any of a wide range of medical, social, legal, interpersonal, and vocational consequences associated with alcohol use and might possibly have engaged in multiple attempts to cut back or control his/her alcohol use. Further, some individuals with an alcohol use disorder are known to continue to use alcohol in spite of an awareness that its use caused or exacerbated a medical condition in their bodies. Braithwaite and Bryant (2010) suggested, for example, that even nonproblematic alcohol use might interfere with the biotransformation of antiviral agents used to treat AIDS, or that the biotransformation process for antiviral agents used to treat AIDS might interfere with the biotransformation of alcohol, resulting in longer periods of intoxication for the individual.

In short, the rare or social drinker is the diametric opposite of the individual who has an alcohol problem, and it is important for the professional working with AUDs to

understand the difference between the individual who rarely drinks or only drinks socially, as compared to the individual with an alcohol problem.

Scope of Alcohol Use in the World Today

It has been estimated that 2 billion people around the world drink alcohol daily (Engel, Green, Voigt, Forsyth, & Kes-havazian, 2015). It is estimated that 52% of the world population age 15 and up have consumed alcohol at some point, and 38.3% have consumed alcohol in the past year (World Health Organization, 2014). In the United States, approximately 80–90% of adults have consumed alcohol at least once, 65–70% have done so in the past year, and close to 51% of the population 12 years of age or older consume alcohol at least once per month (O’Brien, 2006; Sadock, Sadock, & Ruiz, 2015; SAMHSA, 2017; Schuckit, 2010a). It has been estimated that in the United States there are 136.7 million individuals 12 years of age or older who consumed alcohol at least once in the month prior to the survey (SAMHSA, 2017). Another 12,000 people join this number each day as they take their first drink of an alcohol-containing beverage (Lemonick & Park, 2007).

Over the decades, there has been a marked fluctuation in the per capita amount of alcohol consumed in the United States. In the 1790s, it was estimated that the average American consumed 5.8 gallons of pure ethyl alcohol each year, which by the 1830s had increased to 7.1 gallons (Brust, 2004). In 1920, alcohol consumption was outlawed in the United States, and remained illegal until 1933. This forced a reduction in the amount of alcohol consumed, although this is only a guess since so many people were making their own alcohol or buying it illegally. This continues to happen across the world today, where close to 25% of the alcohol consumed across the world is not recorded (World Health Organization, 2014). After the repeal of Prohibition, there was a gradual decline in the amount of alcohol consumed by each person in the United States annually, until the year 1996, when this trend reversed (Naimi et al., 2003). Currently, it is thought that the per capita level of alcohol consumption worldwide is equal to 16 liters of 80-proof vodka, which is equivalent to close to 1.2 ounces a day per each individual 15 and older (World Health Organization, 2014). In the United States, the per capita alcohol consumption is equivalent to 23 liters of 80-proof vodka for each individual over 14 in this country every year (World Health Organization, 2014). This figure pales in comparison to the estimated equivalent 42 liters of 80-proof vodka per individual over age 14 per year consumed in the Republic of Moldova or the close to

40 liters of 80-proof vodka in Russia (World Health Organization, 2014). Even in the normally staid United Kingdom, the level of alcohol consumption is estimated to be the equivalent of 29 liters of 80-proof alcohol per individual over age 14, while in Canada it is estimated to be the equivalent of 25.5 liters of 80-proof vodka per individual over age 14 per year (World Health Organization, 2014). However, considered in a different way, those 15 and over in the United States who actually consume alcohol consume the equivalent of 33.25 liters of 80-proof vodka per year, which is equivalent to over 2 shots (1.5 ounces each) of 80-proof vodka a day (World Health Organization, 2014).

These figures are *averages*, as there is a significant variation in the level of individual alcohol consumption. It has been estimated that just 10% of those who drink alcohol consume 55–60% of the alcohol consumed in the United States each year, while the top 30% of individuals who drink consume 90% of all the alcohol consumed (Aldhous, 2013; Kilbourne, 2002). Beer is the most popular alcohol-containing drink in this country, and spirits come in second, although wine is increasing in popularity (Naimi et al., 2003; World Health Organization, 2014).

The Pharmacology of Ethyl Alcohol

The alcohol molecule is a small, simple molecule, soluble in both lipids and water, although it shows a preference for the latter (Jones, 1996). It might be introduced into the body intravenously, rectally,¹⁸ or as a vapor,¹⁹ but the most common form of alcohol administration is as a liquid consumed orally. Other trends may include “eyeballing,” vaginal administration, or even snorting. When used orally, small amounts of alcohol are absorbed through the mucous membranes of the mouth and esophagus, and 10–20% is absorbed in through the stomach (Sadock et al., 2015; Swift, 2005; Trevejo-Nunez, Kolls, & de Wit, 2015; Zakhari, 2006). The remaining 80% is absorbed through the proximal portion of the small intestine (Schuckit, 2010a; Trevejo-Nunez et al., 2015). Following absorption, the alcohol molecules are rapidly distributed throughout the body, especially to blood-rich organs such as the brain, where the concentration soon surpasses that found

in the blood (Kranzler & Ciraulo, 2005a). This is because alcohol is able to bind to both lipids and water, both of which are found in abundance in the brain. The alcohol molecule does diffuse into **adipose**²⁰ and muscle tissues, but it does so with more difficulty than it does into the tissues of the CNS. Still, this characteristic of alcohol distribution means that a heavier person will have a slightly lower blood alcohol level than a smaller person after consuming the same amount of alcohol.

Following the ingestion of a single drink on an empty stomach, peak blood alcohol levels are achieved in 30 (Knapp, Ciraulo, & Kranzler, 2008) to 60 minutes (Sadock et al., 2015). Some researchers believe that when alcohol is consumed with carbonated beverages, the absorption of the alcohol is more rapid (Sadock et al., 2015; Schuckit, 2008a, 2010a). When mixed with food, especially high-fat foods, the absorption of alcohol is slowed down to the point where peak alcohol levels might not be achieved until 1–6 hours after it was consumed (Baselt, 1996; Cederbaum, 2012; Sher, Wood, Richardson & Jackson, 2005). Thus, by mixing alcohol with food its absorption will be slowed; however, eventually all the alcohol will be absorbed into the body.

In the past, the mechanism through which alcohol induced a state of intoxication was poorly understood, and different theories were advanced to account for alcohol's intoxicating effects (Motluk, 2006). In the early 20th century, it was suggested that alcohol might be able to affect the molecular structure and function of lipids in the neural walls (Brust, 2004; Tabakoff & Hoffman, 2004). This was known as the *membrane fluidization theory*, or the *membrane hypothesis*. According to this theory, alcohol's ability to bind to lipids allowed it to bind to the lipids in the neural walls, making it more difficult for the neurons to maintain normal function. While appealing, this theory is hampered by the facts that: (a) very high concentrations of alcohol are necessary to achieve cellular membrane disruption, and (b) that even small changes in body temperature produce more disruption in cellular membrane integrity than does alcohol (Woodward, 2009). For these reasons, the membrane hypothesis fell into disfavor and there are few advocates of the theory at this time.

Another theory that attempted to explain the effects of alcohol was known as the *TIQ hypothesis*. Trachtenberg and Blum (1987) suggested that alcohol use significantly reduced the brain's production of natural opioid-like molecules known as *enkephalins* and *dynorphins*. Further, during the process of alcohol biotransformation, an alcohol metabolite and naturally occurring neurotransmitters combined to form the toxic

¹⁸This is a rarely utilized method of alcohol administration. Alcohol is easily absorbed through the tissues of the rectum when used as an enema. However, it is exceptionally difficult to titrate the dose and there is a significant risk of serious, possibly fatal, overdose when administered in this manner (Northcutt, 2008). This method of alcohol administration is *not* recommended by the author or publisher of this text.

¹⁹Although devices have been introduced to take advantage of this characteristic of ethyl alcohol, many states have banned their use, and others are expected to do so soon.

²⁰See Glossary.

compound *tetrahydroisoquinoline* (TIQ) (Blum, 1988). TIQ was thought to bind to the opioid receptor sites within the brain's reward system, causing euphoria and a sense of well-being (Blum & Payne, 1991; Blum & Trachtenberg, 1988). However, TIQ's effects are short-lived, a characteristic that would force the individual to continue to drink to maintain the initial feeling of well-being achieved through alcohol use, according to the authors.

Over time, heavy habitual alcohol use was thought to cause the brain to reduce its production of natural opioid-like molecules as the ever-present TIQ was substituted for these natural neurotransmitters (Blum & Payne, 1991; Blum & Trachtenberg, 1988). The individual's cessation of drinking would result in a lack of stimulation in the reward system, which the individual would experience as "craving" for further alcohol use. While the TIQ theory had many proponents in the latter part of the 20th century and still is occasionally suggested as accounting for alcohol-induced feelings of euphoria experienced by individuals who drink alcohol, a number of studies have failed to find evidence supporting the TIQ hypothesis, and it has been found that changes in diet can also induce the same changes in TIQ as observed following alcohol ingestion (Woodward, 2009). There are few advocates of this theory now.

Scientists now believe that alcohol is a "dirty" compound. It alters the action of various neurotransmitters and interferes with the action of messenger molecules within the neuron itself (Heilig & Spanagel, 2015; Knapp et al., 2008; Lovinger, 2008).²¹ Some of the neurotransmitter systems altered by the ingestion of alcohol include (Cruz, Bajo, Schweitzer, & Roberto, 2008; Heilig & Spanagel, 2015; Knapp et al., 2008; Lehne, 2013) GABA_A, glutamate, nicotinic, cannabinoid, opioid, and voltage-gated calcium ion channels. Its effects on the *N-methyl-D-aspartate* (NMDA) receptor sites in the CNS utilized by the neurotransmitter glutamate are especially relevant to how it effects the body (Heilig & Spanagel, 2015; Lehne, 2013; Schuckit, 2008a). **Gamma-amino-butyric acid (GABA)**,²² the main inhibitory neurotransmitter in the brain, binds at one of the subtypes of the NMDA receptor. When alcohol molecules bind at the GABA^{a-1} receptor, it enhances the influx of chloride atoms into the neuron, slowing the rate at which the neuron can fire (Tabakoff & Hoffman, 2004). When the alcohol molecules bind at the GABA^{a2s} receptor site, this induces a subjective sense of relaxation. When alcohol binds to the GABA^{a5s} and the serotonin 5HT₃ receptor site in

sufficient quantities, it can induce memory loss, a loss of inhibitions, psychomotor impairment, and indirectly causes the release of dopamine, which contributes to the experience of alcohol-induced euphoria (Lehne, 2013; Motluk, 2006; Tabakoff & Hoffman, 2004).

When the individual drinks enough alcohol to achieve moderate to high blood levels, the alcohol molecules are known to promote the binding process at the mu opioid receptor site²³ (Cruz et al., 2008; Modesto-Lowe & Fritz, 2005; Stahl, 2008). The mu opioid receptor site appears to be associated with the experience of alcohol-induced euphoria, an observation supported by experimental research that suggests that the administration of opioid antagonists like Naltrexone reduce alcohol consumption by individuals who regularly misuse alcohol. In contrast, the activation of the sigma opioid receptor site by high doses of alcohol appears to be associated with the aversive effects of alcohol (vomiting, etc.).

Technically, alcohol intoxication is an acute confusional state reflecting cortical dysfunction (Filley, 2004; Schuckit, 2006a). At mild to moderate intensities, this cortical dysfunction can result in neuromuscular dysfunction, cognitive dysfunction, and speech problems. When consumed in sufficient quantities, alcohol is capable of interfering with the formation of memories in the individual's brain. This condition is called a **blackout**, although the technical term for it is **anterograde amnesia** (Ghoneim, 2004a, 2004b; Heilig & Spanagel, 2015). At its extreme, it can involve the inability of the individual to remember events for extended periods of time while drinking. More common is the experience of "**gray amnesia**" (or "gray out"), a condition in which individuals have some limited memories of events that transpired while they were intoxicated, intermixed with periods of total amnesia (Heilig & Spanagel, 2015). However, there is little evidence to suggest that social drinking is associated with the long-term neurocognitive changes found in those who drink alcohol on a persistently heavy basis (Rourke & Grant, 2009). Even social drinking can be fatal, though, if the individual experiences cardiopulmonary arrest, which can be the outcome of the rapid intake of large amounts of alcohol.²⁴

The Biotransformation of Alcohol

The liver is the primary organ that biotransforms alcohol, and the primary method of biotransformation is oxidation (Sadock et al., 2015; Schuckit, 2010a; Zakhari, 2006).

²¹To illustrate how little is known about alcohol and its effects, it was recently discovered that alcohol molecules alter the norepinephrine receptor sites in the brain.

²²See Glossary.

²³Discussed in Chapter 11.

²⁴Often seen at college parties where individuals who are inexperienced with alcohol consume large amounts of alcohol in short periods of time, exposing themselves to toxic, potentially fatal levels of alcohol as it is absorbed into the body.

However, about 10% of the alcohol ingested is excreted unchanged or is broken down at other sites in the body (Edenberg, 2007). At extremely high blood levels, the percentage of alcohol that is excreted unchanged through the lungs, urine, and skin is increased, giving the intoxicated person the characteristic smell of intoxication (Sadock et al., 2015; Schuckit, 2006a).

For the individual who only drinks socially on rare occasions, alcohol biotransformation begins in the stomach, which produces small amounts of an enzyme known as *alcohol dehydrogenase (ADH)* (Cederbaum, 2012; Sadock et al., 2015). However, the stomach's ability to produce this enzyme is impaired by the concurrent use of aspirin (Schuckit, 2011). Alcohol dehydrogenase production is also dependent on the level of testosterone in the user's blood. Since women generally produce less testosterone than do men, they produce less alcohol dehydrogenase, contributing to the tendency for women to become more intoxicated on a given amount of alcohol than men (Sadock et al., 2015; Swift, 2005). Women also usually have a lower muscle-to-body mass ratio and about 10% less water volume than men (Zealberg & Brady, 1999), factors that also contribute to the tendency for women to become more intoxicated on a given amount of alcohol compared to men.

The liver is where the majority of alcohol is biotransformed. First, the liver produces large amounts of ADH, breaking alcohol down into a metabolite called **acetaldehyde**. It has been suggested that in prehistoric times the liver's ability to produce ADH evolved so that mammals could biotransform natural alcohol when fermented fruits were ingested, or to help the body deal with the small amount of alcohol produced endogenously²⁵ (Jones, 1996). Acetaldehyde has been found to be extremely toxic to the human body (Melton, 2007). Normally, this is not a problem, since the body produces a family of enzymes²⁶ that are collectively known as **aldehyde dehydrogenase**. These enzymes, especially the form known as *aldehyde dehydrogenase-2*,²⁷ rapidly breaks acetaldehyde down into acetic acid, which can be burned by the muscles as fuel (Melton, 2007). Ultimately, alcohol is biotransformed into carbon dioxide, water, and fatty acids (carbohydrates).

²⁵Occasionally, a person arrested for driving while under the influence of alcohol will try to argue that it is because of this naturally occurring alcohol that s/he was intoxicated, and not because s/he had ingested alcohol-containing beverages. Unfortunately, the bacteria in the gastrointestinal tract produce about 1–2 teaspoons of ethyl alcohol in a 24-hour period, which is hardly sufficient to induce intoxication.

²⁶Sometimes referred to as the *ALDHs*.

²⁷Referred to in some of the literature as *ALDH₂*.

The Speed of Alcohol Biotransformation

There is some inter-individual variability in the speed at which alcohol is biotransformed and eliminated (Edenberg, 2007; Zakhari, 2006). However, the average person might biotransform one standard mixed drink of 80-proof alcohol, 4 ounces of wine, or one 12-ounce can of beer every 60–90 minutes (Fleming, Mihic, & Harris, 2006; Nace, 2005b; Schuckit, 2011). Alcohol is biotransformed through a zero-order biotransformation process, so the rate of alcohol biotransformation is relatively independent of the alcohol blood level (Heilig & Spanagel, 2015). Thus, if a person should consume alcohol at a rate faster than the speed of biotransformation, the blood alcohol level will increase. The outcome of this process will be discussed in the section devoted to the subjective effects of alcohol.

The Alcohol-Flush Reaction

After drinking even a small amount of alcohol, between 3 and 29% of persons of European descent and 47–85% of persons of Asian descent experience the **alcohol flush reaction** (Collins & McNair, 2002; Sher & Wood, 2005). The alcohol flush reaction is the result of a genetic mutation that prevents the liver from being able to produce sufficient amounts of aldehyde dehydrogenase, thus allowing high levels of acetaldehyde to accumulate in the person's blood. The individual will experience symptoms such as facial flushing, heart palpitations, dizziness, and nausea, as acetaldehyde levels climb to perhaps 20 times those seen in the normal person who had consumed a similar amount of alcohol. Because the alcohol flush reaction is so uncomfortable, this is thought to be one reason why alcohol use disorders are less common in persons of Asian descent.

The Blood Alcohol Level (BAL)

Because it is not possible to measure the alcohol level in an individual's brain, physicians have to settle for a measurement of the alcohol concentration in the person's blood, or exhaled breath, procedures that provide the **blood alcohol level (BAL)**.²⁸ The BAL is reported in some countries as milligrams of alcohol per 100 milliliters of blood (mg/mL). A BAL of 0.10 would be 1/10th of a milligram of alcohol per 100 milliliters of blood. The BAL provides a *rough approximation* of the individual's level of intoxication and the behavioral effects of alcohol that should be expected from an

²⁸Occasionally the term *blood alcohol concentration (BAC)* is used.

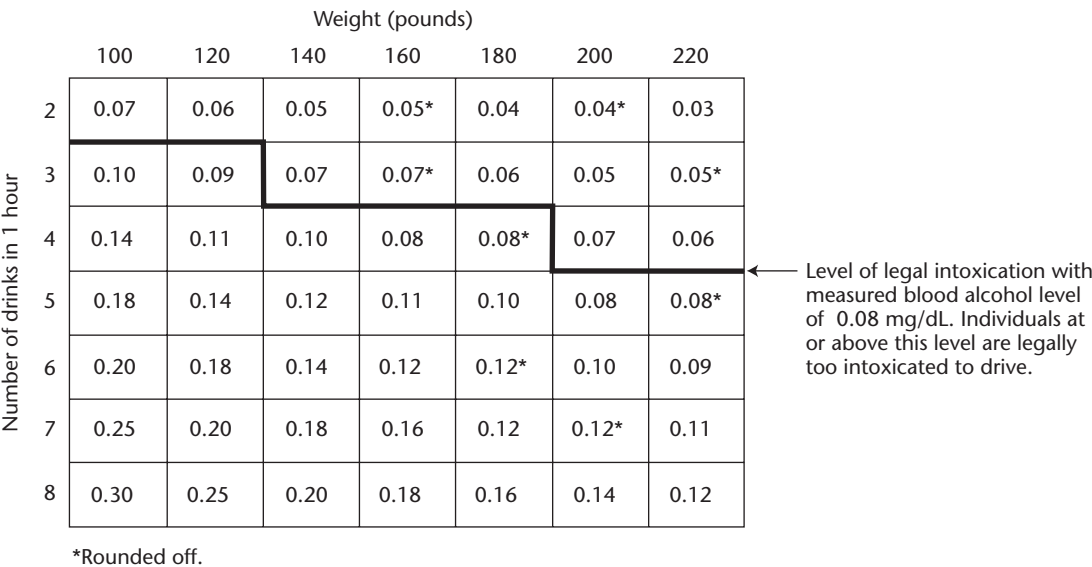


FIGURE 4-1 Approximate Blood Alcohol Levels.

NOTE: The chart is provided only as an illustration and is not sufficiently accurate to be used as legal evidence or as a guide to “safe” drinking. Individual blood alcohol levels from the same dose of alcohol vary widely, and these figures provide an average blood alcohol level for an individual of a given body weight.

individual with the measured BAL (Knapp et al., 2008). The similar terms, *blood alcohol content* or *concentration* (BAC), *breath alcohol concentration* (BrAC), and *blood ethanol concentration* (BEC) are also frequently used to describe alcohol levels. BAC is frequently used to refer to legal limits within blood, whereas BrAC would be legal limits as measured by a breathalyzer. The same individual might have different behaviors at different times with exactly the same BAL in response to different mood states and environmental factors (Stein & Rogers, 2008). Further, the individual’s subjective sense of intoxication appears to be stronger while the BAL is still rising, a phenomenon known as the **Mellanby effect** (Drummer & Odell, 2001; Greenberg, 2010; Sher et al., 2005). The Mellanby effect might reflect the individual’s body starting to become tolerant to the effects of alcohol after even just one drink, although this theory has yet to have sufficient evidence for support.

The concentration of alcohol in the individual’s blood is proportional to the amount of alcohol in the breath exhaled, allowing for the rapid and minimally invasive measurement of the individual’s BAL. Breath alcohol testing is thus preferred over blood tests because of its ease of measurement and accuracy, although blood tests are occasionally used to determine the individual’s BAL.

As noted earlier, the BAL that will be achieved by two people who consume the same amount of alcohol will vary as a result of a number of factors, including whether they had recently had a meal and body size. A hypothetical person who

weighs 100 pounds and who consumed two regular drinks in an hour’s time would have a BAL of 0.09 (just above the amount needed to be legally intoxicated). A second hypothetical person who also had consumed two regular drinks in an hour’s time who weighed 200 pounds would have a BAL of only 0.04 mg/mL however, as the alcohol would be distributed in a larger body volume. Figure 4.1 provides a rough estimate of the BAL that might result if various hypothetical persons of different weights were to consume different amounts of alcohol.²⁹

Subjective Effects of Alcohol on the Individual Who Drinks Socially at Normal Doses

At high doses alcohol is both a neurotoxin and a psychoactive compound (Lezak et al., 2012). It also has a very mild analgesic effect. However, most individuals do not consume alcohol for its analgesic effect but rather for its psychoactive properties. Surprisingly, at low to moderate BALs, the individual’s *expectations* play a major role in how that person interprets the effects of alcohol and his/her drinking behavior (Christiansen, Jennings, & Rose, 2016; Sher et al., 2005).

²⁹This table is provided only to illustrate the process of intoxication at different levels of alcohol consumption, and is *not* intended to function as an aid to diagnosis or as a guide to safe drinking.

TABLE 4-1 Effects of Alcohol on the Infrequent Drinker

Blood Alcohol Level (BAL)	Behavioral and Physical Effects
0.02	Feeling of warmth, relaxation.
0.05–0.09	Skin becomes flushed. Drinker is more talkative, feels euphoria. At this level, psychomotor skills are slightly to moderately impaired, and ataxia develops. Loss of inhibitions, increased reaction time, and visual field disturbances.
0.10–0.19	Slurred speech, severe ataxia, mood instability, drowsiness, nausea and vomiting, staggering gait, confusion.
0.20–0.29	Lethargy, combativeness, stupor, severe ataxia, incoherent speech, amnesia, unconsciousness.
0.30–0.39	Coma, respiratory depression, anesthesia, respiratory failure.
Above 0.40	Death.

SOURCES: Based on Baselt (1996), T. M. Brown and Stoudemire (1998), Brust (2004).

It has been found, for example, that those who use alcohol tend to have more positive expectations for the outcome of their drinking than do individuals who do not drink (Sher et al., 2005). These expectations begin to form early in life, perhaps as early as 3 years of age, and become more entrenched between the ages of 3 and 7 years, well before the individual is old enough to legally consume alcohol (Jones & McMahon, 1998).

One effect that the individual does encounter after just one or two drinks is the **disinhibition effect**. It is believed that this is caused when alcohol interferes with the normal function of the cortex region responsible for inhibitions, as well as abstract thinking and speech. Neurocognitive changes are experienced when the individual's BAL is only 0.02 to 0.03 mg/mL of blood (one to two drinks). This is the dosage range at which the individual also begins to "forget" social inhibitions (Julien, 2005), and might end up doing something that s/he might later regret. The consumption of too much alcohol could lead to the individual's death from respiratory arrest, an outcome that unfortunately is all too common among high school and college students. The effects of alcohol for the individual who drinks rarely or only socially are summarized in the following table:

Powdered Alcohol

Recently, a new form of alcohol has appeared: powdered alcohol. This product is essentially an alcoholic beverage that is freeze dried, producing a powder that when prepared looks like Jell-O® before that product is mixed with water. The powder can be carried in a plastic container and then mixed with water at a time of the individual's choosing. The powder will then dissolve, reconstituting itself into an alcoholic beverage. One brand of powdered alcohol, Palcohol®, was approved for sale in the United States in March of 2015. Each packet will, when mixed with water, provide the individual

with the equivalent of one standard alcoholic beverage. It is too soon to determine whether powdered alcohol will remain a form of alcohol that is only occasionally used under special circumstances where transporting bottles of liquor is difficult or impossible,³⁰ remain a social curiosity, or become a part of a more serious alcohol use disorder in certain individuals. However, legislative efforts have been initiated in several states to ban the sale of this product in those states.

Medical Complications of Alcohol Use for the Individual Who Drinks Socially

A Note of Caution

There are many medical conditions such as diabetes or cardiovascular problems, as well as traumatic brain injuries, that can present as alcohol intoxication (Schuckit, 2011; Shackelford & Nale, 2016). Alcohol intoxication can also interfere with the treatment of a number of medical conditions. Thus, a physician should always determine whether the individual is intoxicated, demonstrating a symptom of another medical condition, or if his or her drinking might complicate the treatment for another disorder.

A Speedy Recovery

Alcohol is biotransformed at approximately the rate of one 12-ounce serving of beer or one standard mixed drink per hour. Many different chemicals or combinations of chemicals have been tried over the years to reduce the period of time that it takes for a given person to recover from the acute

³⁰Such as on a camping trip, for example.

effects of alcohol. What follows is a brief summary of the results of such research.

CAFFEINE

Although it was thought that caffeine counteracted alcohol's sedating effects, research has not supported this (van de Loo et al., 2016); consuming the two together can cause significant health risks, and there is little known about the long-term impact (Robins, Lu, & van Rijn, 2016).

CNS STIMULANTS

Compounds such as cocaine or the amphetamines were once thought to speed recovery from alcohol intoxication. Research has shown that they simply *hide* the behavioral effects of the alcohol in the body, but do not speed up the biotransformation process (Woodward, 2009).

NARCAN®

Based on the assumption that alcohol's euphoric effects are induced by activation of the reward cascade in the brain, it was hoped that Narcan®, a narcotic receptor site blocker used to treat opiate overdoses, might speed the process of recovery from alcohol ingestion. This theory has been found to be unfounded (Woodward, 2009). To date, the only known cure for acute alcohol intoxication is to allow the body to biotransform the alcohol ingested and eliminate it from the circulation.

The Hangover

Approximately 75% of individuals who drink will experience a hangover at some point in their lives, although most people do not experience a hangover every time they consume alcohol (Harbourg, Gunn, Gleiberman, DiFranceisco, & Schork, 1993; Wright et al., 1997). Even small amounts of alcohol can cause headaches in migraine sufferers. Such headaches, while severe, are not *hangovers*. The hangover has been known to be an after-effect to drinking for thousands of years. Physical manifestations of the hangover include fatigue, malaise, sensitivity to light, thirst, tremor, nausea, dizziness, depression, and anxiety (Schuckit, 2006a; Sher et al., 2005). There is evidence to suggest that some individuals are more prone to this alcohol withdrawal effect than others, possibly as a result of genetic variability (Swift & Davidson, 1998).

Once the hangover develops, there is little that can be done to speed its resolution in spite of the wide variety of folk remedies purported to do this (Erickson, 2007). In spite of the individual's subjective discomfort, alcohol-induced hangovers usually resolve in 8–24 hours, and will require only conservative medical treatments such as antacids, bed rest, adequate fluids, and over-the-counter analgesics. Researchers are still divided over the different possible factors

that cause the hangover, including but not limited to (a) the direct effects of alcohol on the individual's brain, (b) the effects of a metabolite of alcohol biotransformation (such as acetaldehyde), (c) some of the flavoring agents mixed with liquors (called **congeners**), (d) an alcohol-induced state of dehydration that affects brain function, (e) an early alcohol-withdrawal syndrome, or (f) the effects of an alcohol-induced reduction in brain β -endorphin levels (Mosier, 1999; Penning, van Nuland, Fliervoet, Olivier, & Verster, 2010; Swift & Davidson, 1998). Some of the congeners contained within alcohol-containing beverages include (Roshenow et al., 2009) acetone, acetaldehyde, tannins, and furfural, although the proportion of these compounds varies from one compound to the next. Bourbon, for example, contains 37 times the concentration of congeners as does vodka (Roshenow et al., 2009). However, the role of congeners in the development of the alcohol withdrawal is still only a theory, and it is possible that another mechanism causes this unpleasant experience.

The Effects of Alcohol on the Cardiovascular System

The question of whether rare social drinking brings with it a cardioprotective effect has proven to be very controversial. The *moderate* use of alcohol, defined as the consumption of no more than two standard drinks per day for a man and half that for a woman, was thought to induce a 10–40% reduction in the individual's risk of developing coronary heart disease (CHD) (Fleming et al., 2006; Klatsky, 2003). Early studies suggested that rare social drinking had a potential cardioprotective effect by increasing levels of HDL cholesterol (the “good” cholesterol) in the blood, making it more difficult for atherosclerotic plaque to build up on the walls of the person's arteries (O'Connor, Rusyniak, & Bruno, 2005). However, “rare social” drinking was defined as significantly lower than the recognized two standard glasses of wine or standard mixed drinks per day each day of the week (Nichols, Scarborough, Allender, & Rayner, 2012). The authors suggested that the safe limit for social drinking was about one-half of a standard glass of wine or mixed drink *per day*.

Chiva-Blanch and colleagues (2012) found that non-alcoholic red wine, which is to say wine with the alcohol removed but the other agents such as the **polyphenols**³¹ left, appeared to provide the cardiovascular protection once attributed to wine. This research, if replicated, suggests a possible approach to the prevention or treatment of cardiovascular disease without exposing the individual to alcohol itself. This apparent cardioprotective effect appears

³¹See Glossary.

to be moderated by the individual's genetic heritage, lifestyle, and current health status, with some individuals obtaining more of a protective effect than others (Britton, Marmot & Shipley, 2008; Hines et al., 2001; Karlamangla et al., 2009).³² The *moderate* use of alcohol is thought to be cardioprotective because it functions as an anticoagulant and reduces fibrinogen levels (Klatsky, 2003). Unfortunately, this cardioprotective effect is achieved at a price, as there is a dose-dependent relationship between alcohol consumption and loss of brain volume that is seen even with just one to two drinks a day (Paula et al., 2008). This effect is stronger in women than in men, but does affect both women and men, according to the authors. Yet meta-analytic data does suggest that moderate consumption (as defined earlier in this chapter) may have cardioprotective effects (Ronsley, Brien, Turner, Mukamal, & Ghali, 2011), and research conducted on close to 62,000 U.S. veterans indicated that moderate alcohol consumption does show a reduction in coronary artery disease (Song et al., 2017). Yet the debate is not yet resolved, as methodological issues continue to be debated and further research is needed to understand the impact of alcohol on cardiovascular health at different levels of drinking (Bell et al., 2017).

Many individuals who binge drink believe that they are immune to the cardiovascular dangers associated with heavy alcohol use³³ because they are only engaging in binge drinking. This belief is wrong: It has been determined that even binge drinking can speed up the formation of plaque in the coronary arteries of an individual (Redmond, Morrow, Kunkiml, Miller-Graziano & Cullen, 2008; Ruidavets et al., 2010). The causal mechanism appears to be that acetaldehyde, an intermediate step in the biotransformation of alcohol, can induce the binding of cells known as monocytes to artery walls, contributing to the formation of plaque in the person's body (Redmond et al., 2008). The research team of Ruidavets and colleagues (2010) compared the incidence of coronary disease in 2,400 men in Belfast, Northern Ireland, where binge drinking was common, to that of 7,340 men in France, where the use of alcoholic beverages was higher but was spread out evenly across the week. They found that males of middle age who binge drink in Belfast were 76% more likely to suffer a heart attack or death from coronary artery disease than individuals in France of the same age group and who also binge drink. This finding is concerning since younger individuals are more likely to engage in binge

drinking. Binge drinking also can increase the risk of a cardiac arrhythmia known as *atrial fibrillation* by about 51% (Kodama et al., 2011).³⁴ A common complication of atrial fibrillation is the formation of blood clots that break loose and might cause either a stroke or a heart attack when they lodge in an artery. The causal mechanism for this unexpected finding is not known at this time, and little is known about the effects of binge drinking in persons at substantial risk for the development of atrial fibrillation due to preexisting cardiovascular disease or diabetes (Liang et al., 2012).

The Effects of Alcohol on the Immune System

There is preliminary evidence that even limited binge drinking (four to five standard drinks) has a time-limited, mild to moderate **immunosuppressant**³⁵ effect on the individual (Afshar et al., 2014; Szabo & Saha, 2015). The duration and strength of this alcohol-induced suppression of the immune system by binge drinking has yet to be determined. However, the fact is that even limited binge drinking should be of concern for individuals whose immune system has been compromised by disease or chemotherapy.

The Effects of Alcohol on the Gastrointestinal Tract

At high blood alcohol levels, the stomach begins to excrete more mucus than normal and will close the pyloric valve between the stomach and the small intestine in an attempt to slow further alcohol absorption. The individual will experience a sense of nausea and might possibly vomit as the body attempts to rid itself of the alcohol, which is after all a poison. Unfortunately, alcohol also interferes with the normal vomiting reflex, possibly to the point where the individual's body might attempt regurgitation while the person is unconscious. This will expose the unconscious person to the danger of possible aspiration of the material being regurgitated, which can contribute to a condition known as **aspirative pneumonia**.³⁶ If the airway should become totally blocked, the unconscious individual might very possibly die during this process. Recent research has also supported the negative impact of alcohol on the microbiome of the intestines (Engen, Green, Voigt, Forsyth, & Keshavarzian, 2015; Hartmann, Seebauer, & Schnabl, 2015).

³²While alcohol use advocates point to this fact as a reason why people should drink alcohol in moderation, they overlook the fact that the French, as a whole, have a higher incidence of alcohol-related liver disease (Walton, 2002).

³³Discussed in the next chapter.

³⁴Sometimes called the *holiday heart syndrome* since many people overindulge by drinking too much on holidays.

³⁵See Glossary.

³⁶See Glossary.

In an interesting small-scale study, 10 individuals considered to drink socially abstained from alcohol use for a month before submitting to a series of blood tests to determine liver function and blood glucose levels, as well as psychological testing to determine concentration skills, work performance, and measures of total sleep time and wakefulness (Coghlan, 2014). At the end of the study it was found that the average abstainer's level of liver fat decreased 15% while their cholesterol level dropped 5%. Even more impressive was the 23% drop in blood glucose levels as well as improved sleep quality and wakefulness (Coghlan, 2014). Although this research was based on a small sample, the dramatic improvements in liver fat level, blood glucose levels, and cholesterol experienced by individuals who drink socially and who abstained from alcohol for a single month hints at even greater benefits for the individual who drinks heavily but learns to abstain from alcohol.

The Effects of Alcohol on Sleep for the Individual Who Drinks Socially

While alcohol, like other central nervous system depressants, might induce a form of sleep, it does not allow the individual to follow a normal sleep cycle. Alcohol-induced sleep problems, while strongest in the individual who drinks to a chronic level,³⁷ can occur even in the individual who drinks only socially, especially after a binge drinking episode (Roshenow et al., 2009; Thakkar, Sharma, & Sahota, 2015). Even modest amounts of alcohol consumed within 2 hours of the initiation of sleep can contribute to both more frequent and longer episodes of **sleep apnea**.³⁸ Alcohol use prior to sleep has been shown to weaken pharyngeal muscle tone, increasing the tendency for the person to snore while asleep, and to experience sleep breathing problems (Qureshi & Lee-Chiong, 2004). Even rare social individuals with known sleep respiratory problems should consult a physician before using alcohol.

Social Drinking and Stroke

While there is evidence that social or light alcohol use (defined as less than two mixed drinks per 24 hours) may reduce the individual's risk for death from coronary artery disease, paradoxically, consumption of less than one standard drink per day has been associated with an increased risk for death from a stroke (Jones et al., 2015; Ronksley et al., 2011).

Alcohol Use and Neurocognitive Effects

There is a growing body of evidence that alcohol can start to induce brain damage even in those who only drink socially. The team of Biller, Bartsch, Homola, and Bendszus (2009) administered either three beers or two glasses of wine to research their participants. The authors then examined the brains of their volunteers through a process known as magnetic resonance spectroscopy, and found that creatine, a chemical that helps to protect neurons, decreases as the individual's blood alcohol level increases. They postulated that this might be one of the mechanisms through which heavy drinking might cause brain damage. Acute intoxication has been identified as a factor in the disruption of the process of neurogenesis in the individual's brain (Crews, 2008). Even social drinking can induce some degree of depression in the individual, possibly at levels that will contribute to self-abusive behavior(s), as evidenced by the fact that as many as two-thirds of those individuals who commit self-injurious acts used alcohol prior to the commission of those acts (McCloskey & Berman, 2003).

The observed neurocognitive deficits appear to persist for hours after the individual's body has finished the process of biotransformation and elimination (Roshenow et al., 2009). In their study the authors found that individuals who binge drank suffered longer reaction times in spite of the participants' subjective belief that they were capable of driving safely. This suggests that individuals who binge drink present a greater risk for motor vehicle accidents than do those who abstain from alcohol or those who choose not to drive the next day.

Other Consequences of Rare/Social Drinking

The most significant of the consequences of rare/social alcohol use is quite simply the death of the individual. Alcohol is responsible for six deaths from chemical overdose every day in the United States (Centers for Disease Control and Prevention, 2015), and close to 6% of all deaths worldwide each year are related to alcohol (World Health Organization, 2014). The amount of alcohol that must be ingested to induce intoxication is already a significant fraction of the lethal dose, and the higher the individual's blood alcohol level becomes, the closer she or he will be to death from an alcohol overdose. Alcohol also interferes with the body's ability to excrete uric acid from the body. This is a matter of some concern for individuals who suffer from high uric acid levels (such as those found in gout and certain forms of kidney stones). The team of Zhang et al. (2006) concluded that even occasional alcohol use would increase the individual's risk of an acute attack of gout if s/he were predisposed to

³⁷Discussed in the next chapter.

³⁸See Glossary.

this condition, with such attacks usually taking place within 24 hours of the individual's alcohol use.

Another possible consequence of social alcohol use is the dreaded “beer goggles” effect (Aldhous, 2008), although evidence for this condition is mixed and might reflect the generalized feeling of well-being achieved through drinking (Maynard, Skinner, Troy, Atwood, & Munafo, 2016). It has been suggested that brief alcohol consumption makes a person less selective in the choice of potential partner(s), resulting in a possible shock when the individual awakens. However, research evidence supporting this theory has been mixed. Further, as noted above, the disinhibition effect of alcohol encourages individuals to engage in behavior(s) they would normally avoid. In 80% of cases where a person was driving while under the influence of alcohol, the individual is found not to be a chronic alcohol user but to have engaged in binge drinking (Quinn & Fromme, 2012). Their binge alcohol use would interfere with their perception of their ability to drive, contributing to their alcohol-related legal problems. Alcohol has been found to interfere with the body's ability to mount an appropriate inflammatory response, possibly contributing to a range of organ damage such as liver disease and breast cancer for the individual (Szabo & Saha, 2015).³⁹ Consumption of just three to six drinks per week results in a 15% increase in the risk for the development of breast cancer, while women who consume 30 or more drinks per week experience a 50% increased risk for invasive breast cancer (Chen, Rosner, Hankinson, Colditz, & Willett, 2011). Thus, even social alcohol use increases the risk of organ damage for the individual.

Paradoxical Rage Reaction

It was once thought that either alcohol alone, or the combination of alcohol with a benzodiazepine, might lower cortical inhibitions to the point where an individual would experience a *paradoxical rage reaction*.⁴⁰ However, the existence of this possible disorder has been challenged by some health care professionals, and it remains a hypothetical construct and not an established diagnosis at this time (Sadock et al., 2015).

Drug Interactions Involving Social Alcohol Use

There has been little research into the effects of social drinking (defined as one to two standard drinks a day) on the

action of various pharmaceutical agents (Breslow, Dong, & White, 2015; Weathermon & Crabb, 1999). It is known that since alcohol functions as a central nervous system (CNS) depressant, it might potentiate the effects of other CNS depressants such as over-the-counter/prescribed antihistamines, benzodiazepines,⁴¹ barbiturates,⁴² opioids,⁴³ and various anesthetic agents used in medical practice (Weathermon & Crabb, 1999; Zernig & Battista, 2000). Patients who take nitroglycerin, used to treat certain heart conditions, should not use alcohol under any circumstances, as the combination of these compounds can cause a significant, potentially serious, drop in blood pressure (Zernig & Battista, 2000).

Patients taking the anticoagulant medication warfarin should not drink, as alcohol's anticoagulant effects will cause abnormal biotransformation patterns in the warfarin being used, with potentially dangerous results for the individual. Also, because of its anticoagulant effects, there is an increased risk of hemorrhage when alcohol is ingested with aspirin. While acetaminophen, a common alternative to aspirin, does not have an anticoagulant effect, the use of acetaminophen and alcohol increases the risk of acetaminophen-related **hepatotoxicity**,⁴⁴ even if used at regular dosage levels (Ciraulo, Shader, Greenblatt, & Creelman, 2006; Woodward, 2009). Thus the use of alcohol with over-the-counter analgesics should be avoided except under the advice of a physician.

Although there is evidence that the antidepressant amitriptyline might enhance the euphoric effects of alcohol, the concurrent use of both medications might cause rapid, potentially dangerous, blood pressure changes for the individual (Weathermon & Crabb, 1999). While the selective serotonin reuptake inhibitors (SSRIs) are antidepressants with fewer side effects or risks than the older antidepressant medications, the use of alcohol with SSRIs increases the individual's risk for the development of the **serotonin syndrome**⁴⁵ (Brown & Stoudemire, 1998). Diabetic patients taking oral medications for their diabetes should not drink, as the alcohol ingested can interfere with the body's ability to biotransform alcohol, and can result in acute alcohol poisoning at even moderate BALs. Further, the antidiabetic medication prevents the body from being able to break the alcohol down, extending the period of alcohol intoxication. Patients on monoamine oxidase inhibitors (MAO inhibitors or MAOIs) should not consume alcohol under *any* circumstances to avoid the risk of

³⁹The topic of alcohol's effects on the body's inflammatory responses is beyond the scope of this text. Szabo and Saha (2015) provide an excellent review of this topic.

⁴⁰Sadock et al. (2015) referred to this condition as *idiosyncratic alcohol intoxication*.

⁴¹Discussed in Chapter 7.

⁴²Discussed in Chapter 6.

⁴³Discussed in Chapter 8.

⁴⁴See Glossary.

⁴⁵See Glossary.

intermixing their medication with the amino acid tyramine. This amino acid is produced during fermentation, and when mixed with an MAOI may cause dangerously high, perhaps fatal, blood pressure levels (Brown & Stoudemire, 1998).

Researchers have found that verapamil hydrochloride⁴⁶ inhibits the process of alcohol biotransformation, increasing the duration of intoxication (Brown & Stoudemire, 1998). Although early research suggested that the medications ranitidine and cimetidine (now sold as over-the-counter agents for the control of stomach acid) should not be mixed with alcohol, later research failed to support this hypothesis. However, mixture of these compounds should be avoided whenever possible. Also, alcohol use should be avoided by persons taking an antibiotic compound such as chloramphenicol, furazolidone, metronidazole, or the antimalarial medication quinacrine. When mixed with these medications, alcohol produces a *flush reaction* type of response that can be both uncomfortable and potentially dangerous. While the antibiotic erythromycin does not cause an alcohol flush reaction response, it does speed gastric emptying, causing abnormally high BALs (Zernig & Battista, 2000). Patients who are on the antibiotic doxycycline and who drink will find that the alcohol decreases the antibiotic blood levels, possibly to the point where it will no longer be effective (Brown & Stoudemire, 1998). Finally, the effectiveness of the antitubercular medication isoniazid (or INH) will be reduced while the patient is drinking, and in extreme cases can induce hepatitis when mixed with alcohol. The list of medications that might interact with alcohol is quite extensive. This is only a partial list of medications that might interact with alcohol. The reader is advised to consult a pharmacist and/or physician before mixing ethyl alcohol with *any* form of over-the-counter or prescription medication.

Alcohol use can interfere with or enhance the effects of many of the drugs that are misused. The concurrent use of alcohol and cocaine interferes with the pharmacokinetics of both compounds, for example. The majority of those who use marijuana may also use alcohol simultaneously, a pattern of substance use that appears to result in higher alcohol intake levels (Subbaraman & Kerr, 2015). This appears to be the reason why individuals who drink and who simultaneously smoke marijuana are approximately twice as likely to drive while under the influence of alcohol as those who only use alcohol (Subbaraman & Kerr, 2015). As is so often the case in the substance use disorders field, there is a need for further research into the effects of simultaneous marijuana and alcohol use. Alcohol is a very potent compound that has

the potential to interact with a wide range of chemicals, and use with other drugs can result in severe, sometimes deadly, consequences.

Alcohol Ingestion and Injury

Pennock (2007) argues persuasively that following World War II, what might collectively be called the “alcohol industry” had adopted several advertising strategies, all of which were designed to project an image of alcohol consumption as a mark of sophistication, a way to share a pleasant time, and a way to entertain guests. Missing from such ./. . . advertisements were admissions that alcohol consumption also played a role in accidental injury, interpersonal violence, and death. Even if the individual whose BAL is between 0.05 and 0.079, levels below that used to define legal intoxication, have a 546% higher risk of being in a motor vehicle accident if s/he were to drive, while a BAL of 0.08 increases the odds of that individual being in a motor vehicle accident by 1,500% (Movig et al., 2004). A recent study found that 37% of drivers who died in single vehicle fatal accidents had blood alcohol levels above the legal limit of 0.08, while 25% tested positive for at least one illicit drug⁴⁷ (Romano & Voas, 2011).

Alcohol use has also been found to be a factor in 51% of all boating fatalities (Copeland, 2011). Ethyl alcohol use has also been found to be a factor in 17–53% of all falls, and 40–67% of all fire-related fatalities (Lewis, 1997). Although bicycling is not usually thought of as a high-risk activity, 32% of the adults who die in a bicycle accident were found to have alcohol in their systems at the time of their accident (Li, Baker, Smialek, & Soderstrom, 2001). This is consistent with the observation that 52% of patients treated at one major trauma center were found to have alcohol in their blood at the time of admission (Cornwell et al., 1998), since bike accidents are one potential form of major trauma. This list, while incomplete, does demonstrate that even casual alcohol use carries with it a significant risk of accidental injury or death.

There is a known association between alcohol use and interpersonal violence. It has been suggested that the alcohol-related disinhibition effect might explain, in part, the relationship between alcohol use and aggressive behavior. Alcohol was found to be involved in 38% of loud arguments, 57% of disputes that involved a threat being made, and 68% of those in which there was physical aggression of some kind (Giancola et al., 2009). In approximately 86% of homicides, 60% of sex offenses, 37% of physical assault, and 30% of child abuse, the perpetrator was under the influence of

⁴⁶A “calcium channel blocker” used for control of hypertension, and sold under the a variety of brand names.

⁴⁷These two subgroups overlapped somewhat and were not mutually exclusive.

alcohol at the time of the offense (Greenfield, 2007; Parrott & Giancola, 2006). Further, an unknown percentage of victims in each category of crime identified above was also using alcohol. The association between alcohol use and injury is so strong that Reynaud, Schwan, Loiseaux-Meunier, Albuissou, and Deteix (2001) recommended that any patient who has been injured while under the influence of alcohol be assessed for an alcohol use disorder (discussed in the next chapter).

As this information suggests, while alcohol is man's most popular recreational beverage, its use is not without significant danger. Alcohol is not as innocuous as many both in and outside of what might loosely be called the "liquor industry" would have us believe. It interacts with numerous pharmaceuticals, and its habitual use is responsible for death from various forms of organ failure as well as accidents.

Alcohol Use and the *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition)⁴⁸

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) identified five alcohol-related disorders, of which two are relevant in this chapter: (1) *alcohol intoxication*, and (2) the *unspecified alcohol-related disorder*. If the premise

⁴⁸The material presented here is to illustrate the relationship between the alcohol use disorders and the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition). This material should not be interpreted as, nor should it be used as, a diagnostic guide.

is that the post-drinking "hangover" is a form of alcohol withdrawal, then (3) this category also applies to a number of individuals discussed in this chapter. The term **alcohol intoxication** reflects those individuals whose drinking has resulted in the state of intoxication discussed in this chapter. Unspecified alcohol-related disorders are beyond the realm of social drinking, and identify individuals who are experiencing occupational, social, familial, psychological, or financial problems due to their drinking but who do not meet the criteria for alcohol use disorder.⁴⁹

Chapter Summary

Although people consume ethyl alcohol as a recreational substance, research has shown that its use carries with it a significant potential for harm. It may be the first recreational chemical produced by humans, and over the years its production has become more sophisticated, moving through the use of fermented honey, to fermented fruits, and on to distilled spirits. Distillation allowed manufacturers to increase the alcohol content in the beverage being produced above the 15% limit imposed by nature itself, allowing more concentrated beverages with higher alcohol contents to be developed. Alcohol's effects on the individual who drinks socially were reviewed, and some of the interactions between alcohol and pharmaceutical agents were discussed. In the next chapter, the effects of chronic and heavy alcohol use will be explored.

⁴⁹This term is discussed in the next chapter.

The Alcohol Use Disorders

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 5.1 Understand what constitutes an AUD and who might be the typical individual with an AUD
- 5.2 Comprehend the complications of the chronic use of alcohol
- 5.3 Understand the differences between chronic use of alcohol and social drinking
- 5.4 Describe the alcohol withdrawal syndrome
- 5.5 Understand the DSM criteria for alcohol-related disorders

Introduction

The focus of the last chapter was on the effects of ethyl alcohol on the individual who might only rarely drink or only drinks socially, in which it was discovered that even limited alcohol use is associated with an increased risk of premature or accidental death. However, the spectrum of alcohol use does not stop with the rare or social use of alcohol; rather, the continuum of alcohol use extends to include alcohol misuse and addiction. A full understanding of the neurological mechanisms that encourage excessive alcohol consumption are not known at this time, although the release of endogenous opioids has long been accepted as a possible mechanism that promotes continued excessive alcohol use. However, research suggests that the ingestion of even small amounts of alcohol by those who drink heavily initiates the release of larger amounts of the endogenous opioids than is true for those who only rarely or socially drink (Mitchell et al., 2012). The implications of such discoveries are only now being explored by clinical researchers.

Psychosocial explanations for alcohol misuse or AUDs vary from individual to individual: Some persons enjoy its euphoric effects, while others misuse it because they believe that they need alcohol to cope with the pain of living. Many have misused alcohol for so long that they have now become physically addicted to it. In this sense, the misuse of alcohol might be viewed as a *common end point* reached by a variety of paths. The consequences of heavy alcohol use make it more harmful to the individual than cocaine or heroin (Nutt, King, & Phillips, 2010), and alcohol use ranks among the leading causes of preventable death around the world (Mitchell et al., 2012). In this chapter, we will examine the problem of heavy, regular alcohol use and the consequences of its misuse.

A Working Definition of the Alcohol Use Disorders

In the previous chapter, individuals with an alcohol use disorder were said to experience any of a wide range of medical, social, legal, interpersonal, and vocational consequences associated with heavy alcohol use and might possibly have engaged in multiple attempts to cut back or control their alcohol use. Further, individuals with an alcohol use disorder are known to continue to use alcohol in spite of an awareness that its use caused or exacerbated a medical condition in their bodies.

This definition includes a wide range of drinking behaviors, and thus clearly needs to be considered as a spectrum. Some persons will drink solely on weekends, abstaining from alcohol during the work week to avoid causing issues with work. Others will abstain from alcohol during work hours, but will start to consume alcohol after the end of the work day, and possibly throughout the weekend. Yet other individuals will intermix periods of heavy alcohol use with periods of lower use, or possibly even abstinence. Some individuals will “hide” their drinking behavior(s) from significant others, while still others will openly consume alcohol abusively, demanding that family/friends accept their drinking as a price for their presence. The common element to all of these different drinking styles is the misuse of alcohol, possibly to the point where the individual becomes physically dependent on it.

It is generally accepted by health care professionals that the consumption of 16 ounces of an 80–100 “proof” liquor, or 11–15 twelve-ounce cans of beer each day for 2–3 weeks will produce a physical dependency on alcohol (Perry, Alexander, Liskow, & DeVane, 2007). The body will have attempted to compensate for the constant use of alcohol during this period, and upon cessation or significant reduction of alcohol intake, the compensatory mechanisms will then cause a characteristic alcohol withdrawal syndrome (AWS). The person with an AUD typically will experience any of a wide range of medical, social, legal, or vocational consequences associated with heavy alcohol use. This person would possibly have engaged in multiple attempts to cut back or control his or her alcohol use. Such individuals might have continued to use alcohol in spite of an awareness that its use caused or exacerbated a medical condition in their bodies. The formal diagnosis of alcohol use disorder is made on the basis of the diagnostic criteria in the current edition of the *Diagnostic and Statistical Manual of Mental Disorders* published by the American Psychiatric Association (2013), which includes a total of 11 criteria, although only two need to be met for an individual to be diagnosed with a mild AUD.

Scope of the Problem

Currently, Europeans have the dubious distinction of being the heaviest drinkers in the world (World Health Organization, 2014). Each year close to 6% of the global population, or 3.3 million people, lose their lives to alcohol-related illness or injuries, a death toll that is approximately half of that wrought by tobacco-related illness (“First shots in the war on alcohol,” 2009; World Health Organization, 2014). Of this number, the highest death toll is related to cardiovascular diseases and diabetes, which account for 33% of the deaths (World Health Organization, 2014).

In the United States, it is thought that 80% of all individuals over age 12 have consumed alcohol at some point in their lives, and that 57.1% of adults used alcohol in the previous month (SAMHSA, 2016, 2017). Further, it is estimated that close to 27% of adults in the United States drank to the point of intoxication at least once in the past month (SAMHSA, 2016). While these statistics would suggest that AUDs are widespread, in reality only a minority of these individuals have an alcohol use disorder. Recent research, focused on the DSM-5 criteria specifically, found that perhaps 29.1% of adults will meet diagnostic criteria for an AUD at some point in their lives, with an estimate of 13.9% meeting criteria in a given year (Grant et al., 2015), although SAMHSA (2017) has a more conservative estimate of 5.6% in 2016. Given that AUDs are a spectrum, only 3.4% of adults would be in the category of severe in a given year, whereas 3.2% would have a moderate AUD, and 7.3% would fit in the mild category of AUDs, although lifetime prevalence shows a different pattern: 13.9% severe, 6.6% moderate, and 8.6% mild (Grant et al., 2015).

To complicate matters, a person’s alcohol use pattern does not remain stable over the course of his or her lifetime. Rather, there are several different pathways that a person’s alcohol use pattern might follow. Some individuals who misuse alcohol continue to do so throughout life, while others alternate between periods of misuse of alcohol interspaced with periods of abstinence or controlled drinking (Hasin, Stinson, Ogburn, & Grant, 2007). Some individuals who drink heavily “mature out” of their misuse of alcohol in this way,¹ learning either to drink socially at appropriate levels of alcohol use, or to abstain from further alcohol use. Some individuals who once met the diagnostic criteria for alcohol use disorder based on their past drinking patterns might currently be abstinent from alcohol use. Some individuals who have been heavy drinkers might be abstinent

¹As will be discussed in Chapter 21, this pattern is often seen in young adults and in college students who misuse alcohol for a period of time, then set it aside when they assume the duties and responsibilities of young adulthood.

due to situational stressors, such as being under court supervision or at risk for losing their job, but without any desire to stop drinking once the external motivation for abstinence is removed.

A popular misconception of the individual who drinks heavily is to picture a person who is unemployed and who spends much of the day sitting on the curb drinking cheap whiskey from a bottle wrapped in a brown paper bag. In reality, the majority of persons with AUDs live lives that appear on the surface to be successful and productive (Aldhous, 2010), making it difficult to identify the majority of those who have AUDs.

The consequences of alcohol use disorders become increasingly severe as the frequency and intensity of the individual's alcohol use increases, or, said another way, as the severity of the AUD moves up the spectrum from mild to moderate or severe. Alcohol-dependent persons are thought to lose about 15 years of potential life as a result of their AUD (Schuckit, 2006a). The economic impact of the alcohol use disorders in the United States alone is estimated to be \$234 billion a year, with 13% of this amount being just for health care costs for persons injured or ill as a result of their alcohol abuse or addiction (Rehm et al., 2009). The authors suggested that the financial cost of the AUDs is between 1 and 6% of the gross national product in the United States. The AUDs are also associated with problems in the interpersonal, educational, vocational, educational, and legal spheres of functioning, problems that indirectly add to the economic impact of the

AUDs. Globally, alcohol causes over 5% of disease and injury and 4% of deaths (World Health Organization, 2014).

Who Is the Typical Person with an Alcohol Use Disorder?

This is a difficult question to answer, in part because alcohol use disorders take so many different forms. Individuals who misuse alcohol are thought to be predominately male, as evidenced by 12-month prevalence of AUDs in males at 17.6% versus 10.4% in females (Grant et al., 2015). Table 5-1 provides an overview of the subtypes of persons with alcohol use disorders.

Individuals with severe AUDs in the United States may experience their first psychosocial or medical problem as a result of their drinking in their twenties or thirties, and they will probably enter treatment for the first time when they are in their forties (Schuckit, 2006a). Although this data would suggest that it is easy to identify adults with AUDs, they are “masters of denial” (Knapp, 1996, p. 19). When confronted, many persons with an AUD are able to offer a thousand and one reasons why they cannot possibly have an alcohol use disorder. Such excuses may include the fact that they are nothing like the “skid row” daily drinker, that they hold a regular job, that they always go to work, that they can tell you the names of 10 people who drink 10 times as much as

TABLE 5-1 Subtypes of Alcohol Use Disorders

Subtype of AUD	Percentage of Sample	Significant Probability of the Following	Select Characteristics
Nonproblematic	68		Low tendency to exceed limits, possible family history.
Moderate	25.6	Age between 20 and 40, likely male, smoker, gambling, use of cannabis	Likely to have some endorsement of use in larger amounts and longer periods than intended, likelihood of using in hazardous situations, inability to stop or reduce. Exceeding drinking limits highly probable, and low likelihood to seek help. Some familial history of AUDs, misuse.
Severe	5.4	Above, plus use of opioids, major depressive disorder, and separated/divorced	Likelihood of scoring high on 6 AUD criteria, including: use of alcohol in hazardous situations; use in larger amounts and longer periods, inability to stop or reduce, and significant likelihood of exceeding limits; low likelihood of seeking help; possibility of significant health consequences; possible history of alcohol use disorders in family of origin; moderate rates of depression.
Extreme	1	Age between 20 and 40, history of suicide attempt(s), smoker, gambling, major depressive disorder, use of tranquilizers	Familial history of alcohol use disorders in many cases. High likelihood of endorsing all 11 criteria for AUD.

Based on Casey, Adamson, and Stringer (2013).

TABLE 5-2 Effects of Alcohol on the Chronic Drinker

Blood Alcohol Level (Bal)	Behavioral and Physical Effects
0.05–0.09	None to minimal effect observed.
0.10–0.19	Mild ataxia, euphoria.
0.20–0.29	Mild emotional changes. Ataxia is more severe.
0.30–0.39	Drowsiness, lethargy, stupor.
0.40–0.49	Coma. Death is possible.
0.50–0.60	Respiratory paralysis that may result in drinker's death. ^a

^aBrust (2004) discussed how, on rare occasions, a patient with a measured BAL of up to 0.80 might be alert or conscious, although such exceptions are rare, and usually a BAL of 0.50 is fatal.

SOURCE: Based on information in Baselt (1996); Lehman, Pilich, and Andrews (1994); Morrison, Rogers, and Thomas (1995); Renner (2004a).

they do, that they never go to the bars, etc. In reality, only about 5% of individuals who are heavy drinkers fit the image of the “skid row” derelict (Brust, 2004). Many of those who drink heavily are “high-functioning” individuals, with jobs, families, and a public image to protect (Aldhous, 2010; Benton, 2009). These individuals will often go to great lengths to hide their growing dependence on alcohol from others, even as their personality defenses protect them from being aware of it themselves. It is only in moments of quiet introspection that the drinker might wonder why they do not drink like a “normal person.”² As the disease progresses, these moments of introspection are thought to become increasingly infrequent. As these details suggest, there is no “typical” person with an AUD.

Physical Dependence, Tolerance, and “Craving”³

There are many symptoms which, when present, suggest that the individual who drinks has moved past simple social drinking, or even heavy alcohol use, to the point where s/he has developed a severe alcohol use disorder. Perhaps the most important of these is the development of **tolerance**. As the individual continues to consume alcohol over periods of time, the body begins to adapt to the continuous presence of alcohol. S/he is said to demonstrate tolerance to alcohol. This process reflects the individual's (Swift, 2005) (1) drinking history and (2) genetic inheritance. A person who consumed alcohol four times a week would be less likely to develop the

same degree of tolerance to alcohol's effects than would an individual who consumed the same amount of alcohol daily, for example.

It is not unusual for physicians or drug counselors to have clients report that they needed to drink more to achieve a given level of intoxication than they required in the past (Nelson, 2000). This is often interpreted as a sign of increased tolerance to the effects of alcohol. Tolerance is very energy-intensive and the liver cannot maintain this higher-than-normal speed of alcohol biotransformation for extended periods of time. Eventually, the individual who drinks alcohol on a chronic basis discovers that she or he does not require as much alcohol to achieve a given level of intoxication as when they were younger. At this point, the individual's tolerance to alcohol is said to be decreasing, usually as a result of aging and the accumulated damage to the drinker's liver. This is sometimes referred to as **reverse tolerance**. The phenomenon of tolerance to alcohol is seen by comparing the effects of alcohol on the individual who drinks habitually in Table 5-2 to those in Table 4-1 (previous chapter).

Many individuals with an AUD depend on alcohol for psychological support as well as a means to enhance their ability to cope with the demands of living. Such individuals are said to be **psychologically dependent** on alcohol, believing that they need alcohol in order to relax, engage in intimate relations, sleep, cope with stress, etc. In contrast to this, the phenomenon of **physical dependence** manifests when the individual suddenly stops drinking and experiences the characteristic *alcohol withdrawal syndrome* (AWS) (discussed later in this chapter). When deprived of alcohol, many persons with an AUD begin to “crave” it, seeking another source of alcohol or other substance to return to their previous level of intoxication, or at least avoid the symptoms of AWS.

²Often referred to at 12-step meetings as “Normies.”

³The discussion of a “craving” for a substance is explored in more detail in Chapter 34.

Complications of Chronic Alcohol Use

Alcohol is hardly a harmless recreational chemical. In the United States, alcohol use disorders cause the loss of 2.5 million years of potential life each year⁴ (Gonzales et al., 2014; Trevejo-Nunez, Kolls, & de Wit, 2015). To put this in other terms, those who drink habitually lose up to 25 years of potential life compared with those who do not drink (Sullivan, 2007). Surprisingly, women with an alcohol use disorder appear to have higher mortality rates from alcohol-related illness than do men (Roerecke & Rehm, 2013). Alcohol-related organ damage places a strain on the health care system in this country: There is a dose-dependent relationship between the amount of alcohol ingested by an individual in both the frequency and the length of stay in hospitals (Hart & Davey Smith, 2009).

The question of alcohol-induced organ damage has been supported in research beyond question. However, a variable that has rarely been considered is the effect of *age* on the individual's body. The aging process will itself exact a toll on the individual's body independent of his or her alcohol consumption status. Unfortunately, it is impossible to determine the percentage of the damage observed in a given individual due to the aging process as opposed to the habitual use of alcohol. It is known, however, that those who drink habitually demonstrate a greater number of serious health problems and longer hospital stays than do individuals of the same age who do not drink.

The amount of physical damage that alcohol causes to the body is mitigated or enhanced by one's genetic inheritance. For example, the individual's risk for developing Wernicke-Korsakoff's disorder⁵ is mediated by genetically determined variations in the production of the enzyme transketolase (Rourke & Grant, 2009). This should not be interpreted to mean that individuals who lack predisposing genetic histories are free from the risk of alcohol-induced organ damage. We do not know enough about human genetics to make such a statement. Rather, it should be assumed that like with other aspects of life, the individual's genetic heritage is one factor that influences the potential development of alcohol-induced organ damage.

The Effects of Chronic Alcohol Use on the Digestive System

Alcohol has a profound impact on the digestive system. During the process of distillation, many of the vitamins, minerals, and amino acids found in wine are lost. Where the original

wine might have contributed something to the individual's daily nutritional requirements, even this modest contribution is lost through the distillation process. To complicate matters, the body of the individual who drinks heavily loses some of its ability to absorb needed nutrients from the food that is ingested, adding to the depletion of vitamin and mineral reserves in the body. Further, the end product of alcohol biotransformation results in the formation of carbohydrates, which makes the drinker feel satisfied, not hungry. These are called "empty calories" by nutritional experts, since they contribute nothing to the individual's dietary requirements of protein, amino acids, etc. In severe cases, the individual who drinks daily may obtain up to 50% of his/her daily caloric requirement from alcohol-derived calories rather than more traditional foods (Griffith & Schenker, 2006). Even if the individual should eat a balanced diet, their ability to absorb needed nutrients is often blocked by alcohol, since it interferes with the absorption of nutrients from the digestive system (Fleming, Mihic, & Harris, 2006; Sadock, Sadock, & Ruiz, 2015). One mechanism that causes this is alcohol-induced diarrhea, which interferes with the body's ability to absorb necessary nutrients from food (Brunton, Parker, Blumenthal, & Buxton, 2008). Collectively, alcohol-induced diarrhea, anorexia, and the empty calories that result from alcohol biotransformation contribute to the development of malnutrition for the individual. If the individual's body should become vitamin-deficient, a common outcome of habitual heavy alcohol use, then s/he is said to have developed *avitaminosis*.⁶

Another possible gastrointestinal problem seen in those who drink heavily is the development of an inflammation of the pancreas, a condition known as *pancreatitis*. About 10% of individuals who drink heavily eventually develop pancreatitis (Brunton et al., 2008; Schuckit, 2008a). Alcohol misuse is estimated to be the cause of 33% of cases of pancreatitis in the United States (Lehne, 2013). This condition can develop after a single episode of heavy drinking, but prolonged heavy drinking is the more common cause of alcohol-induced pancreatitis (Brunton et al., 2008). The causal mechanism for alcohol-induced pancreatitis seems to be the exposure of pancreatic cells to alcohol.

Daily alcohol use has been found to increase the individual's risk for developing various forms of cancer. It is estimated that 389,000 new cases of cancer each year are attributable to heavy alcohol use (Druesne-Peccolo et al., 2009). Heavy alcohol use has been implicated in the development of cancer in the oral cavity, pharynx, liver, stomach, colon, rectum, breast, and esophagus (Brunton et al., 2008; Chen, Rosner,

⁴An estimate of the number of years of potential life lost to alcohol-related disease(s) based on the assumption that the average person lives to age 75.

⁵Discussed later in this chapter.

⁶There are a number of causes for this condition, but the chronic use of alcohol is one of the most significant.

Hankinson, Colditz, & Willett, 2011; Druesne-Peccolo et al., 2009). The observed relationship between alcohol ingestion and esophageal cancer is especially important since the long-term survival rate for patients with this form of cancer is quite low (Khushalani, 2008). The combination of cigarette smoking and heavy alcohol use is especially dangerous. Individuals who drink chronically experience almost a six-fold increase in the risk of developing cancer of the mouth or pharynx (Pagano, Graham, Frost-Pineda, & Gold, 2005). While cigarette smoking is associated with a seven-fold increase in such cancers, individuals who drink chronically and who also smoke cigarettes have a 38-fold higher risk of cancer of the mouth or pharynx than do nonsmokers/nondrinkers (Pagano et al., 2005). On a positive note, the individual's risk of developing cancer of the mouth or throat is reduced after 5 years of abstinence, and at the end of 20 years of abstinence is virtually the same as that of a person who never had an AUD (Rehm, Patra, & Popova, 2007).

Other gastrointestinal impacts that can be caused by chronic alcohol use include gastrointestinal perforations (Patil & Namrath, 2015) as well as significant negative impacts on the gut microbiome (Althani et al., 2016).

The Effects of Chronic Alcohol Use on the Liver

The liver is a unique organ, which is sometimes classified as a part of the digestive system and sometimes as an organ apart from the digestive tract. Because of its role in protecting us from the effects of many environmental toxins, it is classified as a separate organ in this text. It is the organ where the process of alcohol biotransformation and elimination usually is carried out. This may be why the liver is the organ most heavily damaged by chronic alcohol use (Sadock et al., 2015). One possible mechanism for alcohol-induced liver damage is the constant exposure of the liver to alcohol (Jaeschke, 2013). Alcohol interferes with the production of the enzyme glutathione, which it produces to protect itself from various toxins. It also is involved in the inflammatory response when tissues are damaged. Individuals who drink heavily demonstrate an 80% lower glutathione level when compared with nondrinkers, suggesting that this is one mechanism by which alcohol (a toxin) is able to damage the liver (Kershaw & Guidot, 2008).

Between 80 and 90% of individuals who drink heavily⁷ will develop an early manifestation of liver disease known as a “fatty liver.”⁸ Individuals who have this condition have a liver

that is enlarged and does not function normally (Bankole & Alt-Daoud, 2005; Jaeschke, 2013). The “fatty liver” can develop after just a few days of heavy drinking (Khan, Morrow, & McCarron, 2009). While there are few physical manifestations of this disorder that the individual might detect, blood tests would reveal abnormalities in the drinker's liver enzymes that suggest liver damage (Schuckit, 2006a). Fortunately, in its early stages, this condition will usually reverse itself with abstinence from alcohol (Khan et al., 2009). Coghlan (2014) reported that measured level of liver fat dropped 15% after just one month of abstinence from alcohol, for example.

Individuals with a “fatty liver” who continue to drink develop a condition known as liver steatosis and are at risk for premature death. Individuals who drink heavily and chronically and who manifest liver steatosis often experience a more severe form of liver damage: **alcoholic hepatitis**. This condition is essentially an extension of steatosis, with the additional symptoms of liver inflammation, pain, the death of liver cells, and development of collagen deposits in the liver (Schuckit, 2006a; Szabo & Mandreker, 2010). Approximately 35–40% of individuals who drink heavily and who have liver steatosis will develop this disorder unless they discontinue or significantly cut back on their consumption of alcohol (Szabo & Mandreker, 2010). The usual patient with alcohol-induced hepatitis develops this condition after about 15–20 years of heavy drinking. Such patients have a high mortality rate and are poor surgical risks because of their hepatitis, especially if the surgeon is unaware of the individual's drinking history, since alcoholic hepatitis can interfere with the body's normal clotting mechanisms (Jaeschke, 2013).

Of those individuals who develop alcohol-induced hepatitis, 10–35%⁹ go on to develop a condition known as **cirrhosis** of the liver (Bankole & Alt-Daoud, 2005; Kar-san, Rojter, & Saab, 2004; Lehne, 2013; Nace, 2005b). In cirrhosis, individual liver cells die and are replaced by scar tissue. While structurally important for helping the liver maintain its shape, scar tissue is nonfunctional. If the level of liver damage is great enough, the body becomes unable to cleanse itself and will eventually die. A physical examination of a patient with hepatitis will reveal a hard, nodular liver, an enlarged spleen, surface blood vessel changes producing “spider” angiomas, tremor, confusion, blood chemistry changes, and in some men testicular atrophy (Nace, 2005b; Schuckit, 2010a). Chronic ingestion of alcohol also can induce changes in the lining of the intestines, allowing certain toxins produced by gram-negative bacteria to enter the circulation more easily (Molina, Happel, Zhang, Kolls, & Nelson, 2010;

⁷Defined here as persons who drink 5+ drinks per day.

⁸Also known as liver *steatosis*, which is a condition in which more than 5% of the liver is made up of fat cells (Griffith & Schenker, 2006).

⁹Khan et al. (2009) reported that up to 70% of patients who develop alcohol-related hepatitis go on to develop cirrhosis of the liver. It is not known why these different authors provided such disparate estimates.

Szabo & Mandreker, 2010). Some clinicians refer to this as a “leaky gut”¹⁰ which also contributes to vitamin malabsorption syndromes observed as a result of the damaged endothelial cells lining the intestines, possibly exacerbating the effects of liver failure (Szabo & Mandreker, 2010).

Although it would seem at first glance that alcoholic hepatitis would predate the development of cirrhosis, some heavy drinkers appear to manifest cirrhosis without previous signs of hepatitis. Alcohol-induced cirrhosis has been documented in people who have consumed as little as two to four standard drinks a day for just 10 years (Karsan et al., 2004), which would seem to be somewhat counterintuitive in that one would expect that it would take a longer period of heavy drinking to cause this level of damage to the liver. This might reflect the effects of **free radicals**¹¹ generated during the process of alcohol biotransformation, which in theory can contribute to the death of individual liver cells and thus initiate the development of liver cirrhosis (Brust, 2004; Walsh & Alexander, 2000). Surprisingly, there is evidence that coffee consumption might reduce an individual’s risk for developing alcohol-related cirrhosis (Klatsky, Morton, Udaltsova, & Friedman, 2006). The authors suggested that the individual’s risk of developing cirrhosis was reduced by 22% for each cup of coffee consumed in a day, although the exact mechanism for this effect is still not clear at this time.

At one point, it was thought that malnutrition was a factor in the development of alcohol-induced liver disease. However, subsequent research has failed to support that hypothesis. Scientists have discovered, however, that persons who have AUDs are at increased risk of contracting the hepatitis C virus.¹² This, in turn, increases the drinker’s risk for eventual development of cirrhosis, and exacerbates the level of damage to the liver. Why persons with AUDs would be at increased risk for hepatitis C infection remains a mystery. It is known that there is a strong relationship between alcohol-induced cirrhosis and the development of liver cancer (Bagnardi, Blangiardo, La Vecchia, & Corrao, 2001; Schuckit, 2006a). However, hepatitis C is also associated with an increased risk of liver cancer, and it is not clear whether this accounts for the association between heavy drinking and the development of liver cancer.

Another factor that influences the course of alcohol-induced cirrhosis is the retention of sodium and water within the drinker’s body, which indirectly affects cardiac function (Nace, 2005b; Schuckit, 2006a). Further, as the liver becomes enlarged in response to inflammation and cellular damage, it

compresses the blood vessels that pass through it. This causes an increase in blood pressure as the heart struggles to maintain circulation, a condition known as *portal hypertension*. The higher pressure levels can cause blood vessels in the esophagus to swell and become weak, forming *esophageal varices*,¹³ which may rupture with little warning. Ruptured esophageal varices are a medical emergency, with a 20–30% death rate even with the best of medical care (Hegab & Luketic, 2001). Between 50 and 60% of those who survive the initial episode of a bleeding esophageal varix will develop a second episode, which will carry with it an additional 20–30% death rate. Afdhal and Curry (2010) reported that in their research sample only 61% of patients who survived one ruptured varix were still alive at the end of one year.

Scientists once thought that chronic alcohol use could reduce the stomach’s mucosal barrier, exposing it to its own digestive juices (Fleming et al., 2006). The stomach itself might become inflamed, a painful condition known as **alcohol-induced gastritis**. Sometimes the individual will develop stomach ulcers, and if an ulcer should form over a major blood vessel in the stomach wall it may rupture, causing bleeding into the stomach. Such “bleeding” ulcers are known in extreme cases to require the surgical resection of the stomach. The individual need not drink heavily to have a higher risk for gastrointestinal bleeding, as it has been found that consuming just three or more standard drinks per day increases the individual’s chance of a gastrointestinal bleed by 300%.

Habitual drinking also contributes to the development of vitamin malabsorption syndromes, leaving the individual at risk for the development of such infections as tuberculosis (TB).¹⁴ In reality, the term *vitamin malabsorption syndrome* is something of a misnomer, since habitual drinkers are known to have trouble absorbing not only vitamins such as vitamin A, vitamin D, and the B family of vitamins, but also calcium, sodium, phosphorus, and magnesium. During the process of biotransformation, glucose is produced. The infusion of glucose into the individual’s circulation will prevent him or her from feeling hungry, but it will not provide the drinker with the necessary nutrients necessary for healthy living. This, in turn, can contribute to a reduction in the effectiveness of the body’s immune system. The effects of alcohol-induced malnutrition may be seen in the fact that there is a 300–700% increase in the risk of death from pneumonia for those who drink heavily as compared to individuals who do not drink (Schirmer, Wiedermann, & Konwalinka, 2000).

¹⁰Technically known as *endotoxemia*.

¹¹See Glossary.

¹²Discussed in Chapter 36.

¹³The singular is an esophageal *varix*.

¹⁴Discussed in Chapter 36.

The individual with an AUD may experience a change in the bacterial growth pattern in the mouth,¹⁵ contributing to the condition known as **glossitis**¹⁶ and to a possible stricture of the esophagus known as **Barrett's esophagus** (Fleming et al., 2006). The latter condition develops after the esophageal tissues have repeatedly been exposed to digestive juices during gastric reflux, as well as a possible traumatic rupture of the esophagus (Brunton et al., 2008), although there have been recent findings negating the contribution of alcohol use to the development of Barrett's esophagus (Thrift et al., 2014; Thrift, Kramer, Richardson, & El-Sarag, 2014). These conditions, however, can further contribute to the individual's failure to ingest an adequate diet, adding to the possible alcohol-related dietary deficiencies. Finally, the misuse of alcohol contributes to a number of metabolic disorders, including the development of type 2 diabetes¹⁷ (Fernández-Solà, 2015; Wannamethee, Camargo, Manson, Willett, & Rimm, 2003). A significant percentage of individuals with liver disease as a result of alcohol consumption are either glucose intolerant or diabetic, conditions that reflect alcohol-related interference with the body's normal glucose control mechanisms. Schuckit (2006b, 2008a) suggested that the diagnosis of true diabetes, as opposed to an alcohol-induced metabolic dysfunction, would require 2–4 weeks of abstinence for an accurate diagnosis to be possible.

Effects of Chronic Alcohol Use on the Circulatory System

Heavy alcohol use increases the individual's risk of coronary heart disease by as much as 600% (Schuckit, 2006a). Although there are many reasons why a person might develop abnormally high blood pressure, or **hypertension**, alcohol misuse is thought to be responsible for 10% of the cases of this disorder seen in the Western world (Lehne, 2013). The chronic use of alcohol exposes the individual to an increased risk of stroke (Chen, Smith, Harbord, & Lewis, 2008; Fernández-Solà, 2015; O'Connor, Rusyniak, & Bruno, 2005). The team of Casolla and colleagues (2012) found that individuals who use alcohol heavily on average experienced a hemorrhagic stroke 14 years earlier than those who do not drink. However, the risk of stroke may not be equal for both sexes. Ikehara and colleagues (2008) examined the health

histories of 34,776 men and 48,906 women in Japan, and found that heavy alcohol use was associated with an increased risk of death from strokes for men but not for women. However, individuals of either sex who used alcohol heavily shared an increased risk of coronary artery heart disease, according to the authors. This might reflect alcohol's ability to increase the blood levels of angiotensin II, a compound that, among other things, causes the blood vessels to constrict. This forces the heart to expend extra energy to pump the blood through the constricted blood vessels, contributing to an individual's possible hypertension (Kershaw & Guidot, 2008). These statistics suggest that the individual's increased risk of a stroke might outweigh any benefit that s/he might gain from using alcohol to reduce cardiovascular risk.

It has been found that the habitual use of alcohol can induce damage to the muscle tissues in the body, although the exact mechanism is still not clear (Lindsay, Bone, & Fuller, 2010). Virtually every individual who drinks heavily will demonstrate some degree of alcohol-induced muscle damage on special tests (Figueredo, 1997; Lee & Regan, 2002). It is for this reason that alcohol is said to be *cardiotoxic*, although it can also cause damage to other muscle groups in the body. Alcohol inhibits the synthesis of proteins in the muscles, including proteins necessary for normal cardiac muscle function (Ponnappa & Rubin, 2000). Up to a quarter of individuals who drink chronically will develop early onset cardiovascular disease, and clinical cardiomyopathy is thought to be present in 25–40% of individuals who drink chronically (Schuckit, 2006a). It does not take a huge amount of alcohol to induce damage to the muscles of the body, including those of the heart. The ingestion of six cans of beer a day, or a pint of whiskey a day, may induce permanent damage to muscle tissues, and if the cardiac muscle tissues are involved, this will result in a general weakening of the heart muscle (O'Connor et al., 2005; Schuckit, 2005, 2006a, 2006b). Statistically, alcohol use disorders are the most common cause of cardiomyopathy in the United States (Lehne, 2013). Between 40 and 80% of those individuals with alcohol-induced cardiomyopathy will die within 4 years of being diagnosed with this disorder if they continue to drink (Brust, 2004; Figueredo, 1997; Stoschitzky, 2000).

The Effects of Chronic Alcohol Use on the Central Nervous System (CNS)

Although it is often assumed that the liver would be the first organ to be damaged by the chronic use of alcohol, this is not always true. The CNS often is the first organ to demonstrate evidence of alcohol-related damage. The exact mechanism(s) by which heavy alcohol use causes damage to the central nervous system is not fully understood at this time, but may

¹⁵If, as Ackerman (2012) described, microorganisms contribute to the body's ability to cope with stress, extract nutrients from food, and possibly even contribute to our actions, then one must wonder what impact the abnormal bacterial growth patterns found in chronic alcohol abusers will ultimately have on the individual's behavior.

¹⁶See Glossary.

¹⁷Once referred to as "adult onset" or "non-insulin dependent" diabetes.

reflect such factors as (Hermens et al., 2013; Rosenbloom & Pfefferbaum, 2008) age of alcohol use onset, the amount of alcohol consumed over the life span, the individual's pattern of alcohol ingestion, the frequency and intensity of alcohol withdrawal episodes, and the individual's genetic heritage.

Research has shown evidence of alcohol-induced memory deficits after as little as one drink. Fortunately, the individual normally needs to consume more than five standard drinks in an hour's time, producing a blood alcohol level of 0.14–0.20, before alcohol is able to significantly interfere with the process of memory formation and leave gaps in the individual's memory known as **blackouts** (Schuckit, 2011). In an alcohol-induced blackout, the individual may appear intoxicated but conscious to bystanders, answer questions, possibly carry on a coherent conversation, and carry out many complex tasks. However, the individual is later unable to recall part or all of the period of intoxication. The alcohol-induced blackout is a form of **anterograde amnesia** induced by alcohol's ability to disrupt the action of the gamma-aminobutyric acid (GABA) and N-methyl-D-Aspartate (NMDA) in the brain (Nelson et al., 2004). Approximately two-thirds of persons physically dependent on alcohol will report having experienced at least one alcohol-induced blackout (Schuckit, 2008a). The individual's vulnerability to alcohol-related blackouts is influenced by their genetic heritage, with the result being that some individuals are more vulnerable to developing this condition than others (Nelson et al., 2004).

As a group, individuals who chronically misuse alcohol have been found to demonstrate evidence of impaired neurological testing up to 4 weeks after their last drink, and in 10% of the cases the level of neuropsychological impairment is found to be severe (Rourke & Grant, 2009). This impairment in neuropsychological test function appears to reflect the physical damage to the brain found during autopsies or through noninvasive imaging studies such as CT scans or MRI studies. Researchers have found, for example, that up to 50–70% of individuals who drink habitually demonstrate enlarged ventricles (Gilpin & Koob, 2008; Rosenbloom & Pfefferbaum, 2008; Schuckit, 2006a, 2006b). With abstinence, many who drink heavily show evidence of subsequent neural growth on subsequent neuroimaging studies, suggesting that some degree of recovery from alcohol-related neurological damage is possible with long-term abstinence (Schuckit, 2005, 2006a, 2006b). However, it is not clear whether or not an individual who used to drink to excess can return to normal neurological functioning at this time.

Individuals who habitually misuse alcohol demonstrate show evidence of damage to the **prefrontal cortex**¹⁸ region

of the brain (Brunton et al., 2008; Rourke & Grant, 2009). Neuropsychological testing confirms the presence of prefrontal cortex damage in between one-half and two-thirds of those who drink chronically (Zahr & Sullivan, 2008). Another region of the brain that seems vulnerable to alcohol-induced damage is the **cerebellum**,¹⁹ and approximately 50% of individuals who drink heavily show some signs of this damage (Schuckit, 2008a; Tomb, 2008). One percent of individuals who drink heavily and chronically will develop the full **cerebellar atrophy syndrome**. Symptoms of this condition include a characteristic psychomotor dysfunction, gait disturbance, and problems coordinating muscle movements (Berger, 2000; Oehmichen, Auer, & Konig, 2005; Schuckit, 2009).

Chronic alcohol use has been shown to both directly and indirectly alter the function of the visual system. Through the depletion of vitamin stores in the body, it is possible to develop *vitamin deficiency amblyopia*. Symptoms of this condition include blurred vision, a loss of visual perception in the center of the visual field,²⁰ and, in extreme cases, atrophy of the optic nerve, all of which may become permanent in spite of the most aggressive of medical care (Brust, 2004; Lee et al., 2010). These findings are consistent with the observation that alcohol is quite neurotoxic. This neurological damage has been compared with that seen in other forms of neurodegenerative diseases, and is clearly seen in magnetic resonance imaging (MRI) studies of individuals who drink heavily. Such neurodegeneration is observed in those who drink daily and those who binge drink heavily (Crews, 2008). Such studies, while suggestive, cannot determine the exact relationship between habitual alcohol use and neurological damage, since researchers lack pre-drinking neuropsychological test data or radiographic imaging studies to allow them to compare pre- and post-drinking test results (Crews, 2008).

Alcoholism is also a known cause of a form of dementia,²¹ although researchers disagree as to the causal mechanism for this condition. One theory holds that alcohol-induced dementia is the direct result of alcohol's toxic effects on the brain. A second theory is that alcohol-induced vitamin deficiencies are the direct causal mechanism (Berent & Albert, 2005; Filley, 2004). A third theory is that alcohol-induced liver damage results in the brain being chronically exposed to toxins normally filtered from the blood, resulting in neuronal loss. Pfefferbaum, Rosenbloom, Serventi, and Sullivan (2004) suggested that all three of these factors contributed to alcohol-induced neurological damage. Ultimately, the understanding of alcohol's effects on the nerve cells in the

¹⁸See Glossary.

²⁰A condition known as *central scotomata*.

²¹Sometimes called *encephalopathy*.

¹⁸See Glossary.

brain is still under investigation and not fully understood at this time (Collins & Neafsey, 2016).

A limited degree of cognitive function recovery is possible for *some* individuals who drank habitually but who stop drinking; however, maximum recovery might take months (Filley, 2004; Gilpin & Koob, 2008) to years (Rourke & Grant, 2009) of abstinence. However, the degree to which a given individual might recover from such neurological trauma is not known at this time. Many individuals who drink heavily only demonstrate a modest level of cognitive improvement after prolonged periods of abstinence and aggressive vitamin replacement therapies (Mancall, 2008; Schuckit, 2006a). In many cases, the individual is institutionalized because of their memory problems, and 15–30% of all nursing home patients are there because of permanent alcohol-induced brain damage (Schuckit, 2006a). Still, it is possible for some individuals who drank chronically to recover at least some of the cognitive functions lost to heavy alcohol use. Where scientists have identified a degree of brain size reduction in those who drank heavily, after just two months of abstinence, scientists have measured a 1.85% increase in brain volume²² and a 20% improvement in communications efficiency in some (Bartsch et al., 2007). Unfortunately, if the individual should return to the use of alcohol, this recovery in brain function will be lost, and the progression of alcohol-induced brain damage will continue.

Wernicke-Korsakoff's Disease²³

In 1881, the physician Carl Wernicke first described a neurological disorder seen in chronic drinkers that has since been called Wernicke's encephalopathy (Day, Bentham, Callaghan, Kuruvilla, & George, 2004). It was thought that patients with Wernicke's encephalopathy demonstrated a distinctive triad of symptoms of (1) ataxia, (2) mental status changes, and (3) nystagmus or ocular changes (Day et al., 2004; Mattingley & Groon, 2008; Schuckit, 2006a). Now it is known that only 10% of patients with Wernicke's disease demonstrate all three of these symptoms, and that 19% of patients do not demonstrate *any* of these traditionally accepted symptoms. Ninety-six percent of patients with Wernicke's disease will demonstrate nystagmus, but only 87% will experience gait disturbance (Greenberg, 2010). Because some individuals do not demonstrate all the traditional symptoms of Wernicke's disease, it is frequently not diagnosed until post-mortem examination of the body (Kinsella & Riley, 2007; Mattingley & Groon, 2008; Soler-González, Sáez-Peñataro,

Balcells-Oliveró, & Gual-Solé, 2014). In some patients with Wernicke's disease, the only symptoms are irritability and fatigue, or hyperthermia, chronic dyskinesias, and decreased muscle tone in the later stages of the disorder (Mancall, 2008; Mattingley & Groon, 2008; Tse & Koller, 2004).

It must be noted that there are other causes of Wernicke's disorder than long-term alcohol misuse or AUD, such as (Isenberg-Grzeda, Rahane, DeRossa, Ellis, & Nicolson, 2016; Kinsella & Riley, 2007; Mattingley & Groon, 2008) Crohn's disease, anorexia nervosa, AIDS, and cancer. Chemotherapy patients and patients who had gastric bypass surgery are also at risk for this disorder. The causal mechanism for alcohol-induced Wernicke's disease is thought to be **thiamine**²⁴ depletion from the body. The body's thiamine reserves are limited and must constantly be replaced through the individual's dietary intake (Kinsella & Riley, 2007; Soler-González et al., 2014). The poor diet, vitamin malabsorption syndrome, and tendency to rely on alcohol-based calories rather than to ingest a normal diet all interfere with the individual's ability to maintain adequate thiamine levels. The individual's genetic heritage has also been suggested as a factor that might influence the development of thiamine depletion (Mancall, 2008). Vitamin depletion is quite rapid and can be detected after just 7–8 weeks of daily heavy alcohol use, although between 30 and 80% of these individuals will not demonstrate signs of Wernicke's disease (Harper & Matsumoto, 2005; Ropper & Brown, 2005).²⁵

The signs of Wernicke's encephalopathy begin to manifest in the first few hours or days after the use of alcohol is discontinued by the heavy drinker (Fernandez, Eisenschenk, & Okun, 2010; Rourke & Grant, 2009). This is the period in which the individual also is experiencing AWS, making the diagnosis and treatment of Wernicke's difficult. Unfortunately, it is estimated that 20% of patients with untreated or inadequately treated Wernicke's encephalopathy will die, usually of cardiovascular collapse (Mattingley & Groon, 2008). It is thus imperative that the body's thiamine stores be replenished as soon as possible. For example, Ropper and Brown (2005) recommended *automatic* intramuscular injections of thiamine, even if the physician only *suspects* the possibility that the patient has Wernicke's encephalopathy. To limit the amount of neurological damage induced by thiamine depletion, the standard treatment protocol calls for intramuscular injections of 100 mg of thiamine for three days, followed by oral supplements of thiamine. However, Mattingley and Groon (2008) suggested that the standard protocol was too conservative and recommended injected doses of 500 mg of thiamine three times daily, for a minimum of three days, with

²²It is not known whether this increase in brain volume reflects neurogenesis, the development of new dendritic connections between existing neurons, or a combination of these two factors.

²³Called *alcohol-induced persisting amnesic disorder* in some texts.

²⁴See Glossary.

²⁵Another name for the disease that is often used in clinical literature.

concurrent blood tests to determine the individual's magnesium level once daily.

In the early 1900s, before aggressive thiamine replacement therapies were instituted, up to 80% of those patients who developed Wernicke's encephalopathy developed *Korsakoff's syndrome* (Day et al., 2004; Rourke & Grant, 2009). These conditions were originally viewed as separate disorders, although it is now recognized that Wernicke's disease reflects the acute stage while Korsakoff's syndrome is the end stage of thiamine depletion-induced brain damage. These disorders are now often referred to as Wernicke-Korsakoff's disease or Wernicke-Korsakoff's syndrome. Even with the most aggressive thiamine replacement therapies available, 1 in 500 individuals who drink heavily develops Wernicke-Korsakoff's disease (Schuckit, 2008a).

At least 10% of those individuals who develop Wernicke-Korsakoff's will be left with permanent memory impairment (Fernandez et al., 2010; Rourke & Grant, 2009). It was long thought that one of the characteristic symptoms of Korsakoff's syndrome was the inability to acquire new information, or anterograde amnesia. Some degree of retrograde amnesia is also present in many cases, although long-term memory is relatively resistant to alcohol-induced memory loss (Lezak, Hannay, & Fischer, 2004; Mancall, 2008). The individual will be able to recall events from his or her distant past, although possibly with some degree of confusion, but will be unable to retain new information (Mancall, 2008). It is not unusual for those with severe AUDs with alcohol-related memory loss and/or organic brain damage to show a marked indifference to their plight. When faced with evidence of a memory loss, they have been known to provide the assessor with "memories" of a past that never took place, a process known as **confabulation**²⁶ (Mancall, 2008; Ropper & Brown, 2005). In the past, confabulation was viewed as one of the diagnostic criteria for patients with Korsakoff's disorder. Mancall (2008) suggested that confabulation reflects *suggestibility* in the patient: When the medical staff ask the patient a question in a manner that s/he interprets as requiring an answer, the patient manufactures one to please the inquirer. While dramatic, it should be noted that not every patient with Wernicke-Korsakoff's will confabulate (Brust, 2004; Ropper & Samuels, 2009), and, when present, it is usually seen in the earlier stages of Wernicke-Korsakoff's disease (Rourke & Grant, 2009).

In extreme cases of Wernicke-Korsakoff's, the patient will appear almost to be "frozen" in time. The neurologist Oliver Sacks (1970) offered the example of man who was unable to recall anything that had transpired after the late 1940s. If asked, the patient would answer the question as if s/he were still living in the late 1940s and was unable to assimilate information from after that point. The author

of this text interviewed several such individuals during the 1980s. These individuals expressed surprise upon being told that astronauts had visited the moon, that President John F. Kennedy was assassinated, etc. These are extreme examples of this process, and most patients with alcohol-induced amnesia will be able to remember some of the past while being unable to recall other events from their past.

There is some research data suggesting that the chronic use of alcohol does not directly destroy neurons so much as induce a *disconnection syndrome* in which the neural connections between neurons are destroyed (Harper & Matsumoto, 2005). Since neurons require regular stimulation, it is thought that the isolated neurons begin to wither and eventually die, accounting for the neural loss observed in the brains of those who chronically misuse alcohol. However, these theories need further research.

Persistent heavy use of alcohol has also been identified as a risk factor for the development of a movement disorder known as **tardive dyskinesia (TD)** (Lopez & Jeste, 1997). TD is a common complication seen in patients who were treated with neuroleptic drugs for the control of psychotic disorders for extended periods of time, but is occasionally found in individuals who drink chronically and who have never been exposed to neuroleptic agents (Lopez & Jeste, 1997). The causal mechanism for this neurological condition as a result of chronic drinking is not known at this time, but when it does develop in someone who drinks heavily, it is usually only after 10–20 years of heavy alcohol consumption (Lopez & Jeste, 1997).

Alcohol's Effects on the Sleep Cycle

There is still a great deal to be discovered about the impact of alcohol on the normal sleep cycle, although it is known that the chronic use of alcohol interferes with the normal sleep cycle (Conroy, Arnedt, & Brower, 2008; Karam-Hage, 2004; Thakkar, Sharma, & Sahota, 2014). Individuals who drink heavily report that they require more time to fall asleep, and that their sleep is both less sound and less restful than that of nondrinkers the same age (Karam-Hage, 2004). Approximately 60% of persons with an AUD report symptoms of insomnia (Brower, Aldrich, Robinson, Zucker, & Greden, 2001; Conroy et al., 2008). This may reflect alcohol's ability to suppress the production of melatonin in the brain, and melatonin is involved with maintaining the normal sleep/wake cycle (Karam-Hage, 2004; Pettit, 2000). However, a second hypothesis was offered by Milne (2007), who suggested that individuals who drink heavily tend to overestimate the amount of time necessary for them to fall asleep.²⁷

Alcohol use suppresses rapid eye movement (REM) sleep, which is important to memory formation and maintenance of

²⁶See Glossary.

²⁷See **Sleep latency** in Glossary.

several body systems. This effect is most pronounced in the individual who drinks chronically (Hobson, 2005; Schuckit, 2008a). About 85% of our dream experiences take place during REM sleep, and by suppressing the individual's REM sleep cycles, alcohol will interfere with the individual's cognitive function during his/her waking hours. Further, if REM sleep is suppressed by extended periods of alcohol misuse, the individual will spend more time in the REM sleep stage when s/he finally does stop drinking (Irwin, Bjurstrom, & Olmstead, 2016). This phenomenon is known as **REM rebound**. During REM rebound, the individual will experience longer, more intense REM dreams, which are often difficult for the newly abstinent drinker to separate from reality (Ropper & Brown, 2005). Some of these dreams might be so intense and so frightening for the dreamer that they can serve as a relapse trigger for the individual, who may be tempted to return to the use of alcohol to "get a good night's sleep again." REM rebound has been found to last for up to six months after the individual's last drink (Brower et al., 2001; Schuckit & Tapert, 2004). Other forms of sleep disturbances can continue for up to 1–2 years after the individual's last alcohol use (Brower et al., 2001; Karam-Hage, 2004).

Unfortunately, physicians will often treat persons who complain about sleep problems but who do not reveal symptoms of an AUD for insomnia. But most of the traditional pharmaceutical agents used to treat insomnia have a high misuse potential (Conroy et al., 2008). Karam-Hage (2004) suggested that gabapentin (sold under the brand name Neurontin®) is quite useful as a hypnotic agent in individuals with AUDs, and it lacks the misuse potential found in other more traditional hypnotics. Paradoxically, although alcohol is a known neurotoxin, there is evidence that at some doses it might suppress some of the involuntary movements of Huntington's disease (Lopez & Jeste, 1997). While this is not to suggest that alcohol is an accepted treatment for this disorder, it might account for the observation that patients with Huntington's disease tend to misuse alcohol more often than close relatives who do not have this condition (Lopez & Jeste, 1997).

There is also evidence suggesting that chronic alcohol use can contribute to long-term psychomotor coordination problems (DeWilde, Dom, Hulstijn, & Sabbe, 2007). The authors found that persons with AUDs who had recently gone through detoxification required longer to complete psychomotor tasks than would normally be expected. There was some degree of improvement in the speed of psychomotor responses as the individual abstained from alcohol for longer and longer periods of time, but even persons who had been abstinent from alcohol for extended periods still required longer periods of time to complete assigned tasks than were required by their nondrinking peers.

The Effects of Habitual Alcohol Use on the Peripheral Nervous System

The human nervous system is usually viewed as two interconnected systems: the central nervous system (CNS) and the peripheral nervous system (PNS). Unfortunately, alcohol-induced avitaminosis involves both subunits of the nervous system. One of the most common manifestations of alcohol-induced nervous system is *peripheral neuropathy*. This condition develops in 15% (Schuckit, 2005, 2008a; Tomb, 2008) up to possibly 66% (Mellion, Gilchrist, & De La Monte, 2011) of individuals who drink chronically. Symptoms of peripheral neuropathy include feelings of weakness, pain, and a burning sensation in the affected region of the body at the time of onset, followed by a loss of sensation in the peripheral regions of the body (Ropper & Brown, 2005).

The causal mechanism for alcohol-induced peripheral neuropathies is not fully understood. The individual's genetic predisposition appears to be one factor that influences the development of peripheral neuropathies. Other possible factors that appear to influence the development of alcohol-related peripheral neuropathies include the effects of chronic alcohol exposure, and possibly alcohol-related dietary deficiencies. It is thought that alcohol's ability to deplete the body of the B family of vitamins is a major factor (Levin, 2002; Mellion et al., 2011; Tomb, 2008), although stress hormones also seem to be involved (Ferrari, Levine, & Levine, 2013).

The Effects of Alcohol Use Disorders on the Individual's Emotions

Individuals who chronically misuse alcohol are subject to a wide range of psychiatric problems including depression, which is seen in approximately 40% of cases (Schuckit, 2008a). Anxiety is seen in 10–30% of these individuals (Schuckit, 2008a). This anxiety might take the form of a generalized anxiety disorder, or panic attacks (Schuckit, 2005, 2006a, 2006b). Some of these symptoms are secondary to the process of alcohol withdrawal, as evidenced by the fact that up to 80% of patients going through alcohol withdrawal report symptoms of anxiety (Schuckit, 2005, 2006a, 2006b). However, alcohol-induced anxiety is also common, and some individuals turn either to further alcohol use, or to **anxiolytic**²⁸ medications to help control what is perceived as a subjective sense of anxiety. Newly abstinent patients who report anxiety symptoms may require as long as two weeks for complete sobriety before their need for anti-anxiety medications can be adequately assessed.

It has been discovered that 10–20% of patients with an anxiety disorder will also admit to an AUD (Cox & Taylor, 1999).

²⁸See Glossary.

Conversely, 10–40% of patients in treatment for an AUD will report having an anxiety disorder of some kind (Cox & Taylor, 1999). The diagnostic dilemma for the clinician is complicated by the fact that withdrawal-related symptoms are virtually the same as those experienced by patients having anxiety attacks, or generalized anxiety disorder (GAD) (Cullen et al., 2013; Schuckit, 2005). This determination is further complicated by the fact that individuals who chronically misuse alcohol might experience feelings of anxiety for months after their last drink (Schuckit, 2005, 2006a, 2006b, 2008a). Only a careful diagnostic history will reveal whether the patient's anxiety symptoms predated or followed the development of his/her AUD.

As will be discussed later in this chapter, one of the subjective experiences of the alcohol withdrawal process is a sense of anxiety or dread. Unfortunately, it is not uncommon for the individual dependent on alcohol to discuss his/her “anxiety” symptoms with a general physician without revealing his or her AUD. The physician, believing that s/he is treating the patient's apparent anxiety, will often prescribe a benzodiazepine²⁹ for anxiety control. As will be discussed in Chapter 7, the benzodiazepine molecule binds at the same chloride channel in the neuron as does alcohol, both enhancing the effects of alcohol and providing a pharmaceutical replacement for alcohol. So similar are the two compounds that benzodiazepines have been called alcohol in pill form (Longo, 2005), or “freeze dried alcohol” (McGuinness & Fogger, 2006, p. 25).

Approximately 50% of persons with an alcohol use disorder will struggle with serious depression at some point in their lives (Virani, Bezchlibnyk-Butler, Jeffries, & Procyshyn, 2012), and this is frequently missed by medical practitioners (Hobden, Bryant, Sanson-Fisher, Oldmeadow, & Carey, 2016). This underscores the fact that alcohol use disorders and depression are often intertwined. In most cases, the AUD appears to precede the development of a major depression, strongly suggesting that the individual's alcohol misuse induced the depression through an unknown mechanism (Fergusson, Boden, & Horwood, 2009). These findings are consistent with those of Hasin and Grant (2002), who examined the histories of 6,050 individuals recovering from heavy drinking, and found that these individuals had a four-fold increased incidence of depression as compared to non-drinkers the same age.

Depression negatively influences the individual's ability to benefit from alcohol rehabilitation programs, and might contribute to higher dropout rates for those who do enter treatment (Charney, 2004). Fortunately, alcohol-induced depression will usually moderate or resolve after 2–5 weeks of abstinence. While there is some controversy over whether antidepressant

medications should be used because of this fact, Charney (2004) recommended that every case of depression be aggressively treated immediately. Gianoli and Petrakis (2013) observed that while various classes of antidepressants have been found to be effective in treating depression, the effectiveness of these medications in treating a depressed person with an alcohol use disorder has not been investigated. However, the available evidence does suggest that these medications do not reduce the individual's alcohol intake significantly even when their depression has been adequately treated (Gianoli & Petrakis, 2013).

Although there is a trend for individuals who misuse substances to engage in the use of multiple chemicals either at once or within a short period of time, there is a strong relationship between suicide and the AUDs independent of the individual's possible other substance use history (Kennedy et al., 2015). At least one-third of those persons who do end their lives are thought to have an alcohol use disorder (Connor et al., 2006). Statistical evidence has found that suicide is 58–85 times as likely to take place in individuals who are alcohol-dependent as in those who are not alcohol-dependent (Frierson, Melikian, & Wadman, 2002). It has been estimated that the lifetime risk of suicide for individuals who drink chronically is between 5% (Preuss et al., 2003) and 7% (Conner, Li, Meldrum, Duberstein, & Conwell, 2003), far above the statistical average for suicide in the general population.

Alcohol-related suicides are more likely to occur in late middle adulthood, when the effects of the individual's extended alcohol misuse begin to manifest as physical organ damage (Nisbet, 2000). The team of Preuss et al. (2003) followed a cohort of 1,237 individuals dependent on alcohol for 5 years, and discovered that during this period participants were more than twice as likely to end their lives by suicide as were individuals not dependent on alcohol. The team of Dumais and colleagues (2005) concluded that alcohol's disinhibiting effect, combined with the impulsiveness demonstrated by many of those with a personality disorder, and with the presence of a major depression, were all significant risk factors for suicide in males who drank heavily. The topic of suicide, suicide prediction, and intervention is far too complicated to discuss in detail in this text, as entire books have been devoted to this subject. However, the reader should be aware of the inter-relationship between suicide and alcohol use disorders.

One causal mechanism through which chronic alcohol use might contribute to the increased risk of depression in individuals who drink chronically (with the concurrent risk of suicide in those who are depressed, since this is the most common psychiatric diagnosis in completed suicides) is alcohol's ability to affect dopamine turnover in the brain. The constant alcohol-induced release of dopamine might cause a reduction in dopamine binding sites as the brain attempts to adapt to the constant presence of high levels of this compound (Deserno et al., 2015; Heinz, 2006).

²⁹Discussed in Chapter 7.

The Effects of Habitual Alcohol Use on the Respiratory System

The chronic use of alcohol has been found to both cause and exacerbate **sleep apnea**,³⁰ both during the periods of active alcohol use and for a number of weeks after the individual's last drink (Brust, 2004; Schuckit, 2008a). Sleep apnea itself has been identified as a cause of such problems as poor sleep hygiene, hypertension, depression, reduced concentration, daytime fatigue, and possibly falling asleep while driving. The association between heavy drinking and pneumonia has been recognized for centuries. Individuals who misuse alcohol chronically are at increased risk for *aspiration pneumonia*³¹ and various forms of respiratory failure (Kaphalia & Calhoun, 2013; Kershaw & Guidot, 2008; Schuckit, 2006a). It has been demonstrated that the chronic use of alcohol alters the body's natural defense mechanisms from the mouth down to the alveolar spaces in the lungs, in part by reducing the effectiveness of the **macrophages**³² guarding the lungs (Molina et al., 2010; Trevejo-Nunez et al., 2015).

The Effects of Chronic Alcohol Use on Other Body Systems

The social image of alcohol is that it enhances sexual performance. In reality, individuals who drink heavily have been known to suffer from a variety of sexual dysfunctions, including decreased libido for both men and women as well as reduced vaginal lubrication and menstrual cycle irregularities in women (Brunton et al., 2008; Diehl, Silva, & Laranjeira, 2013; Schuckit, 2011). Men who drink heavily might experience decreased sperm production count and motility, decreased ejaculate volume, and possible impotence³³ (Schuckit, 2006a). As will be discussed in Chapter 17, alcohol use by a woman in pregnancy can have profound, devastating effects for the developing fetus.

There is also evidence that suggests that heavy, regular alcohol misuse will result in calcium loss for both men and women, which then weakens the bones (Jerslid, 2001; Mercer et al., 2012). This will, in turn, increase the person's chances for injury and death when the individual falls or is involved in an automobile accident. Preliminary evidence does suggest that at least some bone loss will be regained with abstinence for males who previously drank, providing yet another incentive for the individual to stop drinking alcohol (Malik, Gasser, Moncayo, Kemmer, & Fleischhacker, 2012). Traumatic brain injuries (TBI) are 2–4 times more common in individuals who drink

as opposed to those who do not drink (Rourke & Grant, 2009). Between 29 and 56% of individuals with TBI who live long enough to reach the hospital³⁴ will test positive for alcohol at the time of admission (Kraus & Chu, 2005; Miller & Adams, 2006).³⁵ The individual's post-injury use of alcohol can both mediate and complicate the patient's recovery from the TBI (Mathias & Osborn, 2016; Miller & Adams, 2006). While it is widely believed that the patient is using alcohol to self-medicate the pain and frustration of the aftereffects of the TBI, research data suggests that in most cases the AUD preceded the TBI (Miller & Adams, 2006).

The AUDs have also been identified as a causal factor in 40–50% of all motor vehicle deaths, and up to 67% of home injuries (Miller, 1999). Close to 50% of injuries related to alcohol do occur at home (Bunker, Woods, Conway, & Usher, 2016). Statistically, the individual who drinks is ten times as likely to develop cancer as someone who does not drink (Ordorica & Nace, 1998). It has been estimated that possibly as many as 3.9% of all cancer-related deaths are alcohol-related (Allen et al., 2009). The alcohol metabolite acetaldehyde is thought to play at least a limited role in the development of some of these forms of cancer (Melton, 2007). Habitual alcohol use appears to facilitate the spread of certain forms of cancer of the breast and colon (Forsyth et al., 2009). Chronic use of alcohol is also implicated as a causal agent in certain forms of gum disease (Schuckit, 2005, 2006a, 2006b). Further, chronic consumption of alcohol interferes with the skin's natural defenses against infection, and it might contribute to longer wound healing times and a higher possibility of complications from skin infections (Trevejo-Nunez et al., 2015).

Chronic Alcohol Use and Medication Abuse

Individuals with an alcohol use disorder are at higher risk for misuse of prescription medications. The teams of McCabe, Cranford, and Boyd (2006) and McCabe, Cranford, Morales, and Young (2006) concluded that persons with an alcohol use disorder are 18 times more likely to misuse prescription drugs than those individuals who do not have an AUD. The younger the individual was at the initiation of alcohol use and the amount of alcohol consumed per episode of alcohol use were found to be positively correlated with the concurrent misuse of prescription medications, with young adults being at highest risk for this problem. Additionally, those who have alcohol use problems are more likely to misuse stimulants for studying at the college level (Arria et al., 2013).

³⁰See Glossary.

³¹Discussed in Chapter 36.

³²See Glossary.

³³Possibly as a manifestation of alcohol-induced peripheral neuropathy, discussed elsewhere in this chapter.

³⁴A significant percentage of patients who receive a TBI die before reaching the hospital.

³⁵Although rare/social drinkers might also suffer TBI, it is less likely to be as a result of their alcohol use, and thus this topic was reserved for this chapter.

Between 25 and 50% of persons with AUDs also have benzodiazepine use disorders (Sattar & Bhatia, 2003). So similar are the effects of alcohol and the benzodiazepines that the benzodiazepines can be substituted for alcohol in situations where it would be unwise to use alcohol. The combination of two CNS depressants such as alcohol and a benzodiazepine also increases the individual's risk for an accidental, possibly fatal, overdose. Thus, the use of these medications by persons with an AUD is not without very real dangers.

The Alcohol Withdrawal Syndrome

The **alcohol withdrawal syndrome** (AWS) begins 6–24 hours after the individual's last drink and is interpreted by health care professionals as proof that the individual has become physically dependent on alcohol (Mirijello et al., 2015). Some indicate that it can begin as late as 1 to 3 days after cessation of alcohol (Jesse et al., 2017). The intensity of the withdrawal syndrome depends on (a) the duration and severity of the individual's alcohol use (Perry et al., 2007), as well as (b) their overall state of health, and (c) any concurrent substance use disorders. In severe cases, the AWS can be life threatening³⁶ (Fadem, 2009). The causal mechanism is the sudden reduction or cessation of alcohol intake after the brain has become tolerant to alcohol. When the alcohol level is markedly reduced, the neurons begin to work erratically because the delicate balance between excitatory and inhibitory neurotransmission processes has been disrupted in the absence of alcohol.

Clinically, AWS is an acute brain syndrome that presents in such a manner that it might be mistaken for such conditions as a subdural hematoma, pneumonia, meningitis, or infection involving the CNS unless the attending physician was aware of the individual's drinking history (Saitz, 1998).³⁷ Once it has been identified as AWS, the severity of the alcohol withdrawal is often assessed with the Clinical Institute Withdrawal Assessment for Alcohol Scale-Revised (CIWA-Ar) (Baron, Garbely, & Boyd, 2009; Maldonado, 2010). This noncopyrighted instrument measures 15 symptoms of alcohol withdrawal, with each symptom being rated for severity, with a maximum score of 67 points. A score of 0–4 is interpreted as minimal discomfort from the AWS; 5–12 points is interpreted as evidence of mild alcohol withdrawal. Patients whose score on the CIWA-Ar is between 13 and 19 points are thought to be in moderately severe withdrawal, while scores of 20 or more points are interpreted as evidence of severe alcohol withdrawal. One advantage

of the CIWA-Ar is that it can be administered repeatedly over time, providing a measure of the client's improvement or deterioration over time. Unfortunately, coexisting conditions such as anxiety disorders might inflate the individual's score on the CIWA-Ar, giving the appearance that their alcohol withdrawal is worse than it appears on this instrument (Spiegel, Kumari, & Petri, 2012). Another defect in the CIWA-Ar is that it does not include the individual's vital signs as criteria for determining the severity of the AWS for the individual, even though the vital signs could serve as an objective measure of the intensity of the AWS (Spiegel et al., 2012).

Mild alcohol withdrawal is marked by symptoms such as agitation, anxiety, tremor, diarrhea, abdominal discomfort, exaggerated reflexes, insomnia, vivid dreams or nightmares, nausea, vomiting, tachycardia, headache, memory impairment, problems in concentration, and possible withdrawal seizures (Kelly & Saucier, 2004; Messing, 2008; Perry et al., 2007). These symptoms begin about 16–24 hours after the individual's last drink, and in mild cases of AWS usually subside within 48–72 hours after that time (Perry et al., 2007). Tremor, often one of the first withdrawal signs noted, is often self-medicated by the individual dependent on alcohol through additional alcohol use.³⁸ It is not uncommon for many individuals who drink heavily to keep a drink, or in some cases even a bottle, next to their bed so that they can have a drink even before getting up for the day. This is often done on the pretense of “helping steady my nerves,” or needing an “eye opener.” However, the reality is that this is the early stage of the alcohol withdrawal syndrome, in which the drinker self-medicates by drinking alcohol immediately upon awakening.

Severe AWS usually begins 8–12 hours after the individual's last drink, although if the patient has suffered significant levels of liver damage, this time might be extended for up to ten days after the individual's last drink (Baron et al., 2009; Maldonado, 2010). Symptoms of severe AWS include all of those seen in mild to intermediate severity cases, but also can include perceptual distortions or frank hallucinations, hyperthermia, sepsis, and cardiac arrhythmias (Brunton et al., 2008). When the individual begins to experience actual hallucinations during withdrawal, the condition is termed **alcoholic hallucinosis**. This condition develops in about 10% of cases of AWS, and usually begins one to two days after the individual's last drink. The hallucinations are usually auditory, consisting of voices that are accusatory, threatening, or that are critical of the individual's past and current behavior (Ali et al., 2011). Normally, the hallucinations resolve in a few hours to six days, although in rare cases they might persist for longer (Jesse et al., 2017; Maldonado, 2010). These hallucinations might be

³⁶All real or suspected cases of alcohol withdrawal should be assessed by and treatment should be carried out under the supervision of a physician.

³⁷This is not to say that these or any range of other life-threatening conditions might not also be present, complicating the task of the attending physician(s) working with a patient experiencing AWS.

³⁸Unfortunately, alcohol withdrawal can also exacerbate tremor caused by other conditions such as Parkinson's disease.

visual, auditory, or in rare cases tactile (Kelly & Saucier, 2004; Olmedo & Hoffman, 2000; Ropper & Brown, 2005). Alcohol withdrawal hallucinations are often quite frightening for the individual who might not recognize the nature of the hallucinations (Tse & Koller, 2004). On occasion, individuals have been known to respond to the hallucinations as if they were actual experiences (Ropper & Brown, 2005), possibly attempting suicide or becoming violent in an attempt to escape from their hallucinations (Soyka, 2000; Tekin & Cummings, 2003).

There is a danger of seizures during the alcohol withdrawal process, especially in the more severe cases. The period of greatest risk for withdrawal-related seizures begins within 24 hours of the individual's last drink and peaks 48–96 hours after that time (Jesse et al., 2017; Maldonado, 2010). Between 2 and 16% of individuals who drink heavily will experience a withdrawal seizure(s) (McRae, Brady, & Sonne, 2001; Perry et al., 2007; Schuckit, 2010a), and in 60% of the cases where an individual does experience withdrawal seizures he or she will have multiple seizures (Aminoff, Greenberg, & Simon, 2005; D'Onofrio, Rathlev, Ulrich, Fish, & Greedland, 1999). In 2–4% of cases the individual had a preexisting seizure disorder. The seizure disorder may have been exacerbated by the alcohol withdrawal process, but it should be remembered that medication compliance is often poor in those who drink heavily, and it is possible that the individual has discontinued taking their anticonvulsant medication(s). Anticonvulsant medications are rarely needed in such cases (Sadock et al., 2015; Schuckit, 2010a), and adequate dosing with benzodiazepines is thought to be the most effective immediate intervention for such seizures. In such cases, the prudent physician will order the appropriate blood tests to determine whether the individual has been taking their medication (Parent & Aminoff, 2008; Perry et al., 2007) and administer the appropriate medications as indicated.

Approximately one-third of those individuals who experience a withdrawal seizure will go on to develop **delirium tremens (DTs)**.³⁹ Persons who have engaged in heavy drinking for as little as 5 years have been known to develop the DTs upon cessation from drinking (Fadem, 2009). The DTs usually develop one to five days after alcohol cessation. Some of the symptoms of DTs include profound delirium, vivid visual hallucinations, agitation, delusional beliefs, terror, fever, hypotension, hyperthermia, peripheral vascular collapse, tachycardia, and possible death (Ali et al., 2011; Greenberg, 2010; Maldonado, 2010; Perry et al., 2007; Traub, 2009). Prior to the development of effective pharmacological interventions, between 10 and 40% of persons experiencing the DTs would die, usually of cardiovascular collapse (Greenberg, 2010; Kinsella & Riley, 2007; Maldonado, 2010; Perry et al., 2007). Even today the DTs carry

a 1–2% risk of death even with the most aggressive medical intervention⁴⁰ (Maldonado, 2010; Perry et al., 2007).

Current medical practice is carried out on the assumption that it is best to block the possible development of the DTs with appropriate doses of benzodiazepines during withdrawal. Drawing on the clinical history of 334 patients in Stockholm, Sweden, Palmstierna (2001) identified five markers that seemed to identify the patient at risk for the development of the DTs: (1) the existence of concurrent infections such as pneumonia during the withdrawal process, (2) tachycardia, (3) signs of autonomic nervous system overactivity in spite of an alcohol concentration at or above 1 gram per liter of body fluid, (4) a history of epilepsy, and (5) a history of having previously experienced the DTs.

Alcohol also inhibits the release of what has been called the *antidiuretic hormone*⁴¹ (ADH), altering the fluid balance in the drinker's body (Brunton et al., 2008). This results in the individual being in a state of fluid depletion while intoxicated, often encouraging further drinking because the person feels "thirsty." With the onset of abstinence, the individual's body will often begin to excrete fluids as a compensatory mechanism for the constant presence of ADH breakdown, putting the individual at risk for electrolyte imbalances. This will further increase the individual's risk for cardiovascular and neurological damage. Such fluid retention and cardiac arrhythmias will require pharmacological intervention to increase the patient's chances of survival. The pharmacological treatment of AWS will be discussed in Chapter 33. Patients going through the DTs are also at high risk for alcohol-related muscle damage and the development of **rhabdomyolysis**⁴² (Richards, 2000; Sauret, Marinides, & Wang, 2002). It is possible that there are other symptoms of the alcohol withdrawal process, but the information reviewed above does provide a fairly comprehensive overview of the dangers of acute AWS.

Extended Alcohol Withdrawal

The period of extended withdrawal might last for 3–12 months. During this time, some symptoms of the acute phase of AWS, such as anxiety, sleep problems, and neuropathies might continue to be experienced by the former drinker (Schuckit, 2005, 2006a, 2006b, 2010a). Other symptoms reported during the extended withdrawal phase include depression, emotional excitability, fatigue, and emotional volatility. Further, during the phase of extended withdrawal the person will be exquisitely sensitive to alcohol use cues that might trigger a return to active drinking. Many of these cues will be found in the individual's environment, making it difficult for

³⁹Once called the "rum fits" (Maldonado, 2010; Ropper & Brown, 2005).

⁴⁰Baron et al. (2009) gave a figure of 5–15% mortality rate from the DTs.

⁴¹Technically, vasopressin.

⁴²See Glossary.

him or her to abstain from alcohol during those first critical months (Schuckit, 2010a). Part of this vulnerability to relapse is mediated by a subjective sense of craving for alcohol that continues long after s/he stopped drinking. This is often referred to as being “thirsty.” During such times, the individual finds him/herself preoccupied with drinking as a result of exposure to drinking-related cues. Such cues include events, times, and other stimuli associated with alcohol use. Surprisingly, the smell of cigarettes often serves as a relapse cue for some individuals. There is also evidence that repeated periods of alcohol use interspaced with alcohol withdrawal may enhance the negative effects of alcohol withdrawal, adding to the individual’s motivation to continue drinking.

Alcohol Use and the Diagnostic and Statistical Manual of Mental Disorders (5th Edition)

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) (American Psychiatric Association, 2013) identified five subforms of the alcohol-related disorders:

- *Alcohol use disorder*
- *Alcohol intoxication*
- *Alcohol withdrawal*
- *Other alcohol-induced disorders*
- *Unspecified alcohol-related disorder*

Because there are no clear boundaries between alcohol use, abuse, and dependence, the categories *alcohol intoxication* and *unspecified alcohol-related disorder* were discussed in the last chapter. *Alcohol withdrawal* was discussed in the context of the rare or social drinker, but not in the context of the chronic drinker, which was done above. These terms will be reviewed from that perspective here. It is of interest to note that the DSM-5 manual does not use the term “alcohol dependence.” This term has been replaced, at least in the DSM-5 manual, with the more ambiguous term *AUD*.⁴³ The diagnostic criteria for AUD has been modified slightly to include cultural and gender-specific issues that might influence an assessor’s perspective of a drinker, but essentially are the same as the criteria used to diagnose alcohol dependence in past editions of the *Diagnostic and Statistical Manual of Mental Disorders*, including but not limited to⁴⁴ tolerance,

failed attempts to quit, “craving” for alcohol, preoccupation with alcohol use, continued alcohol use in spite of physical or interpersonal risks, etc. (American Psychiatric Association, 2013).⁴⁵ Modifiers for the AUD include whether the individual is actively drinking, is remission (with modifiers for early or sustained remission), and whether the individual’s drinking is curtailed because they are in a controlled environment.

The diagnostic criteria for a formal diagnosis of alcohol withdrawal are relatively unchanged from earlier editions of the DSM and will not be discussed further here. The *unspecified alcohol-related disorder* is a transitional category for those individuals whose drinking is clearly beyond that of social drinking, who are experiencing occupational, social, familial, or financial problems because of their drinking, but who not meet the full criteria for alcohol dependence at this time. The *other alcohol-induced disorder* category includes alcohol-induced conditions, which simulate other forms of psychopathology such as a psychotic reaction. These conditions usually resolve within a few days of the completion of the alcohol withdrawal process.

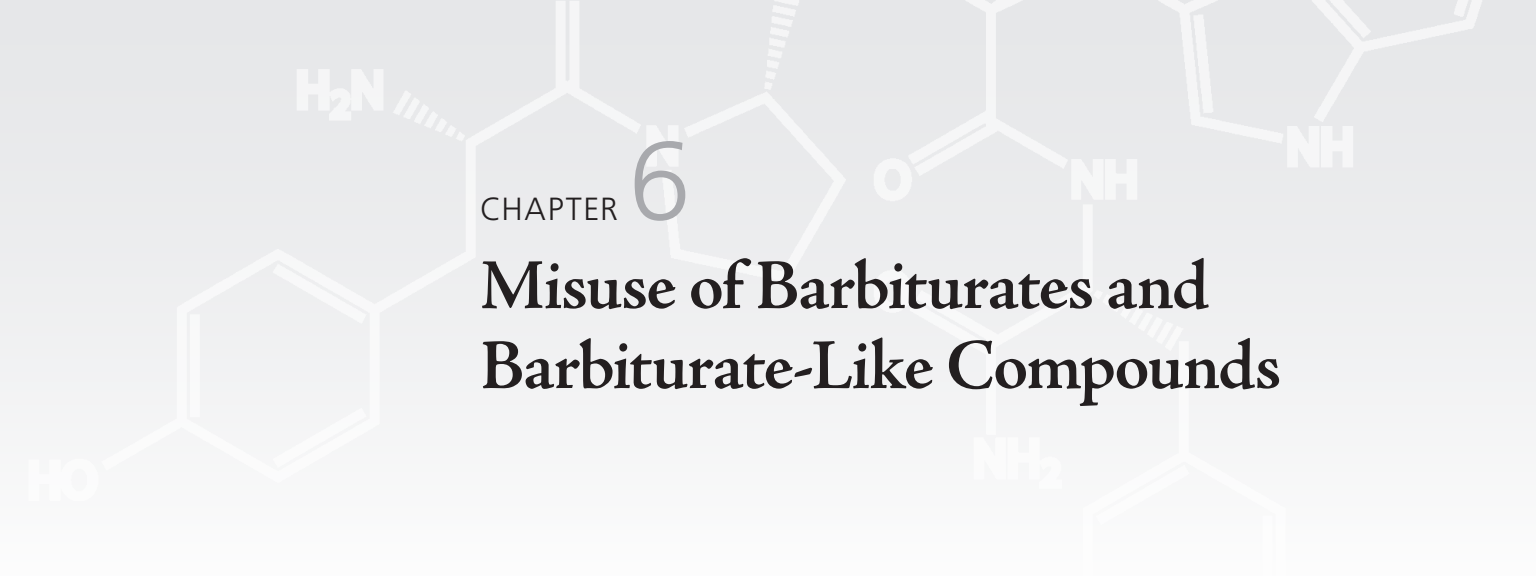
Chapter Summary

Ethyl alcohol is a toxin that affects virtually every organ system when consumed to excess. The brain appears to be especially vulnerable to the negative effects of heavy alcohol use, although the individual’s genetic heritage does influence his or her risk for alcohol-related health problems. In spite of the widespread knowledge that alcohol can induce damage throughout the body, the short-term reinforcement potential of alcohol entices a small percentage of those who consume it to drink to excess. A combination of cultural, genetic, and interpersonal risk factors support or defend against the risk that any given individual will become physically dependent on alcohol. At this point, individuals must go through the “detoxification” process to help their bodies return to normal functioning and minimize organ damage. The severity of the withdrawal symptoms is dependent on the individual’s genetic heritage and alcohol use history. In extreme cases, the severity of the individual’s alcohol withdrawal process will contribute to an organic brain syndrome known as the delirium tremens (DTs). A century ago this condition carried with it a high death rate. Today, even with the most aggressive of pharmacological interventions, the DTs still can result in the individual’s death in some cases, illustrating the neurotoxic effects of alcohol.

⁴³This text uses the same term to denote any problematic alcohol use while the *Diagnostic and Statistical Manual of Mental Disorders*, (5th edition) (DSM-5) (American Psychiatric Association, 2013) apparently uses the term only for what would be called alcohol addiction in this text.

⁴⁴The reader is referred to the *Diagnostic and Statistical Manual of Mental Disorders*, (5th edition) for a full list of the diagnostic criteria.

⁴⁵The full list of the symptoms of an AUD, along with known cultural social and medical modifiers is discussed at length in the DSM-5 manual and the reader is referred to the DSM-5 manual for a more complete discussion of this topic.



CHAPTER 6

Misuse of Barbiturates and Barbiturate-Like Compounds

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 6.1 Understand the history of barbiturates
- 6.2 Understand the pharmacology, subjective effects, and complications of barbiturates at appropriate prescribed levels
- 6.3 Contrast the pharmacology, subjective effects, and complications of above-normal use of barbiturates with normal prescribed levels of use
- 6.4 Describe substances similar to barbiturates

Introduction

Anxiety and insomnia have been problems since at least the dawn of history. For thousands of years, alcohol was one of the few agents that could reduce anxiety or help the individual fall asleep. Anxiety disorders are the most commonly identified form of mental illness, affecting almost 34% of the general population at some point in their lifetime (Bandelow & Michaelis, 2015). Further, possibly up to 22% of individuals struggle with insomnia (Reynolds & Ebben, 2017). However, as discussed in the last chapter, alcohol's effectiveness as an antianxiety agent or hypnotic is both limited and potentially lethal for the user.

At the start of the chemical revolution in the 19th century, chemists began to identify compounds that were able to reduce the individual's sense of dread and induce a form of sleep that was, if not normal, at least was as close to a normal state of sleep as could be chemically induced. These compounds were found to be rather dangerous, but in some cases they also became popular drugs of misuse. In this chapter, we will discuss these various medications, their role in history, and their misuse potentials.

Early Medical Treatment of Anxiety and Insomnia

Many of the early anxiolytic/hypnotic agents introduced in the late 18th and early 19th centuries produced a dose-dependent effect on the user. Depending on the dose administered, the effects could range from sedation, to sleep, to a profound loss of consciousness, a state of surgical

anesthesia, and, ultimately, to death (Mihic & Harris, 2011). The first of these compounds to be introduced was **chloral hydrate**, which was marketed as a hypnotic agent in 1870. Technically, chloral hydrate is a prodrug, which is rapidly biotransformed into *trichloroethanol*, considered the active agent of chloral hydrate, as well as trichloroacetic acid and dichloroacetate after oral administration (Shroads, Coats, Langaee, Shuster, & Stacpoole, 2015). It was administered orally, and a dose of 1–2 grams would cause the patient to fall asleep in less than an hour.

The effects of chloral hydrate lasted for 8–11 hours, making it appear to be ideal as a hypnotic agent. Unfortunately, physicians soon discovered that chloral hydrate had several problematic side effects. Chloral hydrate is quite irritating to the stomach lining, and repeated use over a short period of time might result in significant levels of damage. Also, it was discovered that chloral hydrate is quite addictive, and that the therapeutic dose¹ is only one-half to one-third of the lethal dose (Virani, Bezchlibnyk-Butler, Jeffries, & Procyshyn, 2012). Finally, after it had been in clinical use for some time, physicians discovered that withdrawal from chloral hydrate could result in life-threatening seizures (Brown & Stoudemire, 1998). Chloral hydrate interacts with commonly used anticoagulant drugs such as warfarin, numerous antianxiety and antidepressant drugs, and can alter the biotransformation of numerous other compounds. Fortunately, this medication is only rarely used in helping elderly patients sleep due to the high overdose potential and the speed of dependency development (American Geriatrics Society Beers Criteria Update Expert Panel, 2015), and its use is increasingly rare in the practice of medicine. There have been recent reductions in its use within pediatric medicine for sedation during EEGs (Dirani, Nasreddine, Melhem, Arabi, & Beydoun, 2017), and the oral forms of this substance were discontinued in 2012.

Paraldehyde was first isolated in 1829 and first used as a hypnotic in 1882. It proved to be an effective hypnotic, producing little cardiac or respiratory depression. However, it tends to produce a very noxious taste in the user's mouth, and users develop a strong, unpleasant odor on their breath after ingestion. It is also irritating to the mucous membranes of the mouth and throat, and for these reasons it is usually diluted in another liquid before use. Its therapeutic half-life ranges from 3.4 to 9.8 hours. Between 70 and 80% of a single dose leaves the body unchanged, usually through exhalation, which accounts for the unpleasant odor on the user's breath. Paraldehyde has a misuse potential similar to that of alcohol, and paraldehyde intoxication resembles that of alcohol

intoxication in many ways. After the barbiturates were introduced, paraldehyde gradually fell into disfavor, and is rarely if ever used at this time (Doble, Martin, & Nutt, 2004).

Bromide salts were introduced in the mid-1800s, and in an era before federal oversight of pharmaceuticals they were available without prescription. These compounds were originally introduced as a treatment for epilepsy, and later as sedative and hypnotics (Bisaga, 2008). Soon after their introduction, it was discovered that after a few days' continuous use, a reservoir of these compounds built up in the user's body, causing a drug-induced depression. Bromide salts also had a very narrow therapeutic window, and withdrawal from bromide salts after periods of extended use can include such symptoms as seizures, psychosis, and delirium (Bisaga, 2008). Bromide salts have been totally replaced by newer compounds and are no longer available in the United States for human usage, although they continue to be used in veterinary medicine.

Diphenhydramine is an antihistamine with a strong sedative side-effect. It was first introduced in the 1940s and subsequently marketed as Benadryl® (Hevesi, 2007). Because of the sedation, it is often used as an over-the-counter sleep aid, either by itself or in combination with other compounds. While it has some degree of success in this application, there are risks of anticholinergic-induced delirium in the elderly when misused at higher than normal doses, or when used on a chronic basis (Perry, Alexander, Liskow, & DeVane, 2007).

Despite differences in their chemical structures, all of these compounds are central nervous system (CNS) depressants. The relative potencies of these barbiturate-like compounds are reviewed in Figure 6-1. These various compounds all **potentiate** the effects of other CNS depressants, and they all have misuse potentials equal to if not greater than that of alcohol. Still, these compounds were the treatment(s) of choice for insomnia or anxiety until the barbiturates were introduced in the early 20th century.

History and Current Medical Uses of Barbiturates

In 1864, the German chemist Adolf von Baeyer discovered barbituric acid, the parent compound from which the barbiturates are derived (Nemeroff & Putnam, 2005). Barbituric acid is itself inactive, but derivatives of this parent compound yielded a large family of chemicals that could be used as sedatives, or (at higher doses) hypnotic agents. The first of these compounds, barbital, was introduced in 1903. Within a short period of time, a flood of barbiturates were introduced, so dominating the market that for the first half of the 20th century no non-barbiturate sedative-hypnotic

¹Which is called a "narrow" therapeutic window, as discussed in Chapter 3.

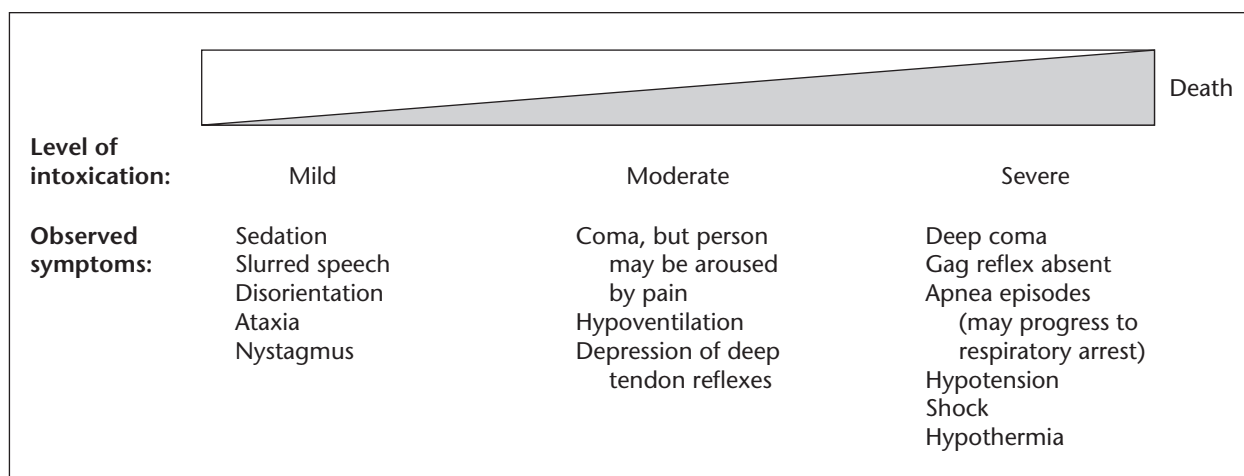


FIGURE 6-1 Relative potency of CNS depressants.

compounds were introduced (Nelson, 2000; Nemeroff & Putnam, 2005). At the height of their popularity, more than *one million pounds* of barbiturate compounds were manufactured each year just in the United States (Brust, 2004). More than 2,500 different barbiturate compounds were developed, although most were never marketed and remained only laboratory curiosities. Only about 50 of these compounds were ever introduced into clinical use, of which perhaps 20 are still used by physicians (Nishino, Mishima, Mignot, & Dement, 2004).

Originally thought to be nonaddictive, clinical experience with these compounds soon revealed the opposite (Ivanov, Schulz, Palmero, & Newcorn, 2006). Legally, barbiturates are classified as Schedule II, III, and IV compounds² and are available only by prescription. After the introduction of the benzodiazepines³ in the 1960s, barbiturates slowly fell into disfavor with physicians, although their use is occasionally encountered (O'Brien, 2011). In addition, there are still some areas of medicine where barbiturates remain the pharmaceutical of choice (Ciraulo et al., 2005). These include certain surgical procedures, treatment of some forms of migraine headache, and seizure control on both an emergency and long-term basis (Gussow & Carlson, 2017; Mihic & Harris, 2011; Nemeroff & Putnam, 2005; Ropper & Brown, 2005). Additionally, there is increased interest in the use of barbiturates for alcohol withdrawal, particularly when the patient does not respond well to benzodiazepines (Askgaard et al., 2016; Martin & Katz, 2016). Controversy still rages around the appropriate use of many of these compounds. Physicians

have long thought that barbiturates were helpful in controlling the swelling of the brain following trauma, although this belief has been challenged (Brain Trauma Foundation, 2000; Majdan et al., 2013; Nemeroff & Putnam, 2005), and there appear to be a number of better alternatives at this point in time (Gruenbaum, Zlotnik, Gruenbaum, Hersey, & Bilotta, 2016). Questions have been raised about their use in inducing a coma in a terminally ill patient who is in extreme pain, and perhaps the most controversial application of the barbiturates is their role in the process of lethal injection of criminals sentenced to the death penalty.

The Misuse Potential of the Barbiturates

The barbiturates have a significant misuse potential, and are quite dangerous to use. In light of all that has been discovered about their misuse potential, it is surprising to learn they have enjoyed a minor resurgence in popularity. Older generations, especially those over the age of 70, became addicted to these compounds decades ago, and often continue to misuse them. This group of compounds has enjoyed an ongoing popularity with some illicit drug users (Ropper & Brown, 2005), and approximately 0.2% of the U.S. population over age 11 struggles with misuse of these substances (SAMHSA, 2017).

Pharmacology of the Barbiturates

There are minor differences in the chemical structure between various members of the barbiturate family of compounds, differences that translate into variations in

²See Appendix 3.

³Discussed in the next chapter.

TABLE 6-1 Clinical Applications of Barbiturates

Duration of Effect	Application
Ultra-short-acting barbiturates	When injected, effects begin in seconds, and last for <30 minutes. Very lipid-soluble. Useful in dental surgical procedures.
Short-acting barbiturates	Usually administered orally. Effects begin in 10–20 minutes and last for 3–4 hours. Elimination half-life may be longer than duration of effect. Lipid solubility falls between that of ultra-short-acting and intermediate-duration barbiturates.
Intermediate-duration barbiturates	Usually administered orally. Effects begin in approximately 1 hour. Effects of a single dose last for 6–8 hours. Elimination half-life may be longer than duration of effect. Moderately lipid-soluble.
Long-acting barbiturates	Usually administered orally. Effects of a single dose begin in about an hour, and last for 6–12 hours. Elimination half-life may be longer than duration of effect. Lipid solubility less than that of intermediate-duration barbiturates.

SOURCES: Chart based on Brunton et al. (2008); Ciraulo & Knapp (2009); Meyer & Quenzer (2005); Mihic & Harris (2011); Zevin & Benowitz (1998).

absorption, distribution, biotransformation, and elimination. However, they all have their main effects in the central nervous system, which is “exquisitely sensitive” (Brunton, Parker, Blumenthal, & Buxton, 2008, p. 270) to the effects of these drugs. Different barbiturate compounds have different degrees of lipid solubility. The barbiturates that have greater degrees of lipid solubility tend to be more potent and have a more rapid onset of action, although they also have a shorter duration of effect than barbiturates with less lipid solubility (Levin, 2002; Ropper & Brown, 2005). This is clearly seen in the difference between the effects of pentobarbital as compared with phenobarbital. A single oral dose of pentobarbital, which is very lipid-soluble, will begin to have an effect in 10–15 minutes, while a single dose of phenobarbital, which is poorly lipid-soluble, might require an hour or more to begin to act on the nervous system.

All the various barbiturates share the same mechanism of action: inhibiting the closing of the GABA_A channel in the wall of many neurons, slowing the rate at which they can establish the electrical differential necessary to fire (Brunton et al., 2008; Ciraulo & Sarid-Segal, 2005; Doble et al., 2004; Lehne, 2013; Nishino et al., 2004). In contrast to the benzodiazepines, the barbiturates can cause this effect even in the absence of the GABA molecule itself (Doble et al., 2004; Gussow & Carlson, 2017; Lehne, 2013; Parrott, Morinan, Moss, & Scholey, 2004).

Clinically, barbiturates are classified by their *duration of action*,⁴ as reviewed in Table 6-1.

In Chapter 3, it was noted that for some compounds, the duration of effect is significantly different than the elimination half-life of that compound, a characteristic found in

the barbiturates. This depends on the ability of the specific barbiturate to form chemical bonds with lipid and protein molecules. Longer-duration barbiturates have greater degrees of protein binding. The short-acting barbiturate *Nembutal*, which begins to take effect on the user in 10–15 minutes after a single dose, lasts for 3–4 hours. However, the molecules of this compound are extensively redistributed around the body following absorption, with the elimination half-life such that 10–50 hours pass before all of a single dose is eliminated (Levin, 2002; Nemeroff & Putnam, 2005). Following absorption, significant amounts of some of the shorter-acting barbiturates are stored in various body tissues and then released back into the general circulation, causing a “hangover” effect. The user will experience reduced psychomotor function for a significant period of time after the desired effects of the barbiturate have ended. Generally, shorter-term barbiturates require biotransformation by the liver before elimination, while long-acting barbiturates are eliminated from the body virtually unchanged. The barbiturate methohexital has a half-life of 3–6 hours and is extensively biotransformed by the liver before elimination. In contrast, phenobarbital has a half-life of 2–6 days and 25–50% of a single dose will be excreted from the body unchanged (American Society of Health System Pharmacists, 2008).

Barbiturates are usually administered orally, although many of the ultra-short-duration barbiturates are used intravenously to rapidly induce anesthesia for surgical procedures. On rare occasions, barbiturates may be administered through suppositories. Orally administered barbiturates are rapidly absorbed through the small intestine (Levin, 2002; Nemeroff & Putnam, 2005). Once in the general circulation, the barbiturate molecules are distributed throughout the body, and the highest concentrations are found in the liver and the brain (American Society of Health System Pharmacists, 2008).

⁴A number of different classification systems for barbiturates have been suggested over the years. This text will follow the system suggested by Zevin and Benowitz (1998).

Behaviorally, the effects of barbiturates are very similar to those of alcohol (Ciraulo & Sarid-Segal, 2005; Nishino et al., 2004). The barbiturates will depress the level of neural activity, as is seen with alcohol ingestion, but they also have a minor impact on the heart, muscle tissues, and the respiration process (Ciraulo et al., 2005). In the brain, the barbiturate molecules tend to have their greatest effect on the cortex, the reticular activating system, and the **medulla oblongata**.⁵ Not surprisingly, these are the neurons with the greatest number of GABA receptor sites, where the barbiturate molecules are therapeutically active. By reducing the level of neural activity in the neurons in the cortex, at low doses the barbiturates are able to induce a sense of relaxation, and at slightly higher doses induce a form of sleep. However, because of their effects on the respiratory center of the brain, high dosage levels of a barbiturate, or lower levels of a barbiturate mixed with other CNS depressants, are capable of causing death from respiratory depression (Lehne, 2013).

The barbiturates have a narrow therapeutic window. Depending on the exact barbiturate molecule involved, the therapeutic window is only 1:3 to 1:10 (Brunton et al., 2008; Ciraulo et al., 2005; Meyer & Quenzer, 2005; Saunders, 2016). In other words, the therapeutic dose is between one-third to one-tenth the lethal dose. Research has revealed that using a barbiturate fewer than 18 times a year still elevates the individual's risk of death from all causes, a risk that increases as the number of doses used by the individual increases (Kripke, Langer, & Kline, 2012). Barbiturate-induced death can occur either as a result of a deliberate act or as a result of dosage miscalculation. It has been estimated that at the height of their popularity, the annual death rate from prescribed barbiturates was 118 for every 100,000 prescriptions (Drummer & Odell, 2001). One reason for this high death rate is that barbiturates were and continue to be used in suicide attempts. This is one reason few physicians continue to prescribe these compounds (Perry et al., 2007).

Subjective Effects of Barbiturates at Normal Dosage Levels

At therapeutic doses, barbiturates cause the user to experience a sense of relaxation, even a sense of euphoria (Ciraulo et al., 2005). Some users also report a sense of sedation or fatigue, drowsiness, ataxia, and an increase in reaction time similar to that seen in alcohol intoxication (Filley, 2004; Nishino et al., 2004). At slightly higher doses, the barbiturates induce a form of sleep. Since both the barbiturates

and alcohol affect the same gated chloride ion channel in the neural wall, the pharmacological mechanism by which they achieve their effects is very similar, and thus the subjective experience is about the same. Indeed, patients who appear intoxicated but who have no sign of alcohol in their bodies should be tested for barbiturate ingestion to rule out this possibility.

Complications of Barbiturate Use at Normal Dosage Levels

Like alcohol, barbiturates interfere with the normal function of the neurons of the cortex, possibly causing a *paradoxical rage reaction* (Ciraulo et al., 2005). Other side effects of barbiturates when used at normal dosage levels include feelings of nausea, dizziness, and mental slowness. But anxious patients report that their sense of anxiety is reduced, if not eliminated, and patients with insomnia report that they can slip into a state of drug-induced sleep. Unfortunately, tolerance to the hypnotic effects of barbiturates will develop after a few days of continuous use (Drummer & Odell, 2001), and while tolerance to the therapeutic dose develops, the lethal threshold for these drugs remains unchanged. If the individual should increase the amount ingested or intermix barbiturates with other CNS depressants in an effort to regain the original anxiolytic or hypnotic effect, it is very possible for the individual to die from an overdose.

Further, the sleep induced by barbiturates is not a normal form of sleep. Barbiturates interfere with the normal progression of sleep stages, and suppress the duration of the rapid eye movement (REM) sleep stage (Nemeroff & Putnam, 2005; Nishino et al., 2004). Following nightly use of barbiturates for as little as two weeks, REM sleep time has been reduced by as much as 50% (Brunton et al., 2008). While reduced REM sleep time for one or two nights is not thought to be dangerous, long-term REM sleep impairment is thought to have long-term emotional and physical effects on the individual. When the barbiturates are discontinued after an extended period of use, they will induce the phenomenon of **REM rebound**,⁶ with dream intensity bordering on nightmares for the individual. These REM rebound dreams may serve as an incentive for the person to return to the use of barbiturates, or similar compounds, to “get a good night’s sleep.”

Barbiturates are able to cause the user to experience a drug-induced “hangover” the next day (Wilson, Shannon, & Shields, 2011). The subjective experience for the user is of

⁵See Glossary.

⁶See Glossary.

“just not being able to get going” if not of continued intoxication by barbiturates. This drug-induced hangover effect is the result of the distribution and elimination characteristics of the barbiturate being used. As was discussed in Chapter 3, physicians estimate that it takes five elimination half-life periods to eliminate a single dose of a compound from the body. However, the extended elimination half-lives of many barbiturates result in significant amounts of the drug remaining in the user's body for hours or days after a single dose. For example, although the therapeutic effects of a single dose of secobarbital might last for 6–8 hours, the hangover effect might cause impaired motor coordination abilities for 10–20 hours after the dose was ingested (Mihic & Harris, 2011). If the person adds to the reservoir of nonmetabolized drug by ingesting additional doses of the barbiturate, there is a greater chance that the individual will establish a reservoir of barbiturates that have not been biotransformed, inducing a drug “hangover.” Individuals with impaired liver function, such as the elderly or persons with advanced liver disease, are especially prone to barbiturate “hangover” effects.

One application of the barbiturate phenobarbital is the control of epileptic seizures in certain patients, although there are a number of alternative anti-epileptic medications that have been introduced in the past decades, and phenobarbital is increasingly being replaced by one or more of these newer compounds (Fallahian & Hashemian, 2017). This is perhaps a good thing, since it has been discovered that persons who have taken phenobarbital for seizure control on a long-term basis suffer an 8-point drop on IQ tests, although it is not clear whether this is an artifact, a drug-induced effect, or the seizure disorder (Breggin, 1999). It also is not known whether this measured loss of IQ is reversible, or if the effect is limited to phenobarbital. The research on the impact of prenatal and early childhood use of barbiturates on development and behavior are still under investigation (Bath & Scharfman, 2013). Other known complications of barbiturates when used at therapeutic doses include sexual performance problems and a loss of libido in both men and women (Finger, Lund, & Slagle, 1997). Hypersensitivity reactions have been reported in patients receiving a barbiturate, especially in patients who suffer from asthma (Mihic & Harris, 2011). Other known complications include nausea, vomiting, diarrhea, skin rashes, and in some cases constipation. Finally, some patients develop an extreme sensitivity to sunlight known as **photosensitivity**, placing them at risk for sunburn after even short exposures to sunlight (Mitkov, Trowbridge, Lockshin, & Caplan, 2014).

Persons who suffer from attention deficit-hyperactivity disorder (ADHD), and who also receive a barbiturate, experience a resurgence or intensification of the ADHD symptoms (Parisi, Moavero, Verrotti, & Curatolo, 2010). This

effect would appear to reflect the ability of barbiturates to suppress the action of the reticular activating system (RAS) in the brain. It is thought that ADHD is caused by an underactive RAS, so any medication that reduces the level of RAS activity will probably intensify the symptoms of ADHD.

Drug Interactions Involving Barbiturates

When used at therapeutic doses, barbiturates are able to potentiate the effects of other CNS depressants, including those of alcohol, narcotic analgesics, phenothiazines, benzodiazepines, and antihistamines. The interaction between the barbiturates and antihistamines is especially problematic, since the latter class of chemicals block the action of histamine, a neurotransmitter that serves an excitatory function in the brain. Patients using monoamine oxidase inhibitor (MAOI) medications should not take a barbiturate except under a physician's supervision, since MAOI inhibitors can block the biotransformation of barbiturates, placing the user at an unintended risk for a barbiturate overdose (Ciraulo, Shader, Greenblatt, & Creelman, 2006; Tatro, 2009). Barbiturates also reduce the effectiveness of the antibiotic doxycycline, and speed up the biotransformation of the class of antidepressant medications known as “tricyclic” antidepressants (Ciraulo et al., 2006). They also speed up the biotransformation of oral contraceptives, corticosteroids, the anticoagulant medication warfarin, and the antibiotic metronidazole. Barbiturates are biotransformed by the same region of the liver that biotransforms the anti-asthma medication theophylline, which may interfere with asthma control. Finally, patients using barbiturates and the over-the-counter analgesic acetaminophen are at increased risk for liver damage (Tatro, 2009). As this list would suggest, the barbiturates are exceptionally potent compounds that should not be intermixed with other medications except under the supervision of a physician.

Effects of the Barbiturates at Above-Normal Dosage Levels

Individuals who ingest higher than normal levels of barbiturates demonstrate slurred speech and ataxia, as well as other behaviors similar to those seen in alcohol intoxication. Barbiturates interfere with the normal cough reflex, placing the individual at risk for conditions such as pneumonia and bronchitis. The barbiturates cause a dose-dependent reduction in respiration, which at its extreme can result in respiratory arrest, as the barbiturates cause the respiratory centers in the medulla oblongata to become less sensitive to the rising blood carbon dioxide levels. Hypothermia is also

seen when the barbiturates are used at above-normal dosage levels (Ciraulo et al., 2005; Pagliaro & Pagliaro, 1998). Other symptoms seen when barbiturates are ingested at above-normal doses include a progressive loss of reflex activity, tachycardia, hypotension, coma, and possible death (Nemeroff & Putnam, 2005).

Although physicians have had access to a range of safer medications, intentional or unintentional barbiturate overdoses are not unheard of. If the overdose victim reaches support before s/he develops shock or hypoxia, there is a good chance that s/he may fully recover from the overdose (Nishino et al., 2005). If only for this reason *any suspected barbiturate overdose should immediately be assessed and treated by a physician.*

Neuroadaptation, Tolerance, and Physical Dependence on Barbiturates

With periods of continuous use, the individual's body will begin a process of **neuroadaptation**,⁷ and over a surprisingly short time, the individual becomes tolerant to many of the effects of the barbiturate. The process of barbiturate-induced neuroadaptation is not uniform, however. For example, when a barbiturate such as phenobarbital is used to control seizures, neuroadaptation does not appear to be a major problem, and after the patient adapts to the sedative effects of the medication, s/he might be maintained on the same dose for extended periods of time without becoming tolerant to the anticonvulsant effects of this medication. In contrast, a person using a barbiturate as a hypnotic might become tolerant to this effect after just a couple of weeks (Nemeroff & Putnam, 2005). Both patients and individuals misusing these substances have been known to try to overcome their increasing tolerance to a given barbiturate by increasing their dose. Unfortunately, in spite of the process of neuroadaptation, the lethal dose of a barbiturate remains relatively unchanged (Lehne, 2013; Meyer & Quenzer, 2005; Mihic & Harris, 2011; Wilson, Shannon, & Shields, 2017). Individuals misusing barbiturates also develop tolerance to the euphoric effects of these drugs, which again might prompt many individuals to increase the dosage level or intermix barbiturates with other CNS depressants. As stated earlier, the outcome of either process might be a fatal suppression of the respiratory reflex. Further, barbiturates have been documented to induce **cross-tolerance**.⁸ Cross tolerance between

alcohol and the barbiturates is common, as is cross-tolerance between barbiturates and narcotic analgesics, as well as the hallucinogen PCP.

The barbiturates are able to induce a state of physical dependence with a characteristic withdrawal syndrome if an individual should discontinue or drastically or reduce his/her barbiturate use. *Barbiturate withdrawal is potentially life-threatening and should be attempted only under the supervision of a physician* (Erickson, 2007; Meyer & Quenzer, 2005; Sadock, Sadock, & Ruiz, 2015; Saunders, 2016). Longer-acting barbiturates will tend to have longer withdrawal periods. The barbiturate withdrawal syndrome is similar to the alcohol withdrawal syndrome, with symptoms including confusion, seizures, muscle weakness, anorexia, muscle twitches, rebound anxiety and trembling, agitation, a delirium tremens-like state, brain damage, and possible death (Ciraulo & Sarid-Segal, 2005; Saunders, 2016). Barbiturate withdrawal seizures may begin on the second or third day of abstinence, and are rare after the twelfth day of abstinence. The acute withdrawal syndrome normally lasts 3–14 days. Physicians may use any of a wide range of pharmaceuticals to help control the severity of the withdrawal process; however, patients should be warned that there is no symptom-free withdrawal.

The Barbiturate-Like Drugs

Because physicians quickly became aware of the many adverse side effects of barbiturates, pharmaceutical companies began to look for substitutes that might be both effective and safe to use. This resulted in a number of compounds that were introduced in the 1950s to replace the barbiturates, including *meprobamate*, *methaqualone*, *glutethimide*, *ethchlorvynol*, and *methypyrrolon*. The chemical structure of some of these compounds (such as glutethimide and methypyrrolon) is very similar to that of the barbiturates (Julien, 2005). Like the barbiturates, glutethimide and methypyrrolon are mainly biotransformed in the liver, and all of these compounds share the characteristic of being global neural inhibitors rather than anxiolytic or insomnia-specific compounds. Although each of these compounds was introduced as “nonaddicting,” subsequent clinical experience demonstrated that each has a misuse potential very similar to that of the barbiturates.

Glutethimide was widely used after its introduction, but soon it became apparent that there were wide variations in its absorption, both between patients and within the same patient over time. Further, users were found to rapidly develop tolerance to its effects, and the discontinuance syndrome was found to be rather severe (Kranzler & Ciraulo, 2005b). Glutethimide withdrawal symptoms can include

⁷If the drug is being abused, the same process is called “tolerance.”

⁸See Glossary.

seizures, tremulousness, nausea, tachycardia, fever, as well as catatonia-like symptoms (Kranzler & Ciraulo, 2005b).

The therapeutic dose of glutethimide is just a little below the toxic dosage range, placing the user at high risk for an overdose. The symptoms of a glutethimide overdose can take up to 120 hours to resolve (Kranzler & Ciraulo, 2005b). Detoxification with controlled doses of a long-term barbiturate such as phenobarbital was recommended at the rate of 60 mg of phenobarbital for each 500 mg of glutethimide ingested daily for stabilization, followed by a gradual reduction in each day's dose of phenobarbital until the patient was drug free (Kranzler & Ciraulo, 2005b). Because of the complications associated with its use, neither ethchlorvynol or glutethimide is used by physicians except under special circumstances (Schuckit, 2006a). The prolonged use of ethchlorvynol can induce a loss of vision known as **amblyopia**, which will slowly clear after the drug is discontinued.

Meprobamate was first introduced in 1955 as a “non-barbiturate” compound that could be used in the daytime to treat anxiety and at higher dosage levels as a hypnotic agent at night. It was also marketed as a muscle relaxant, although its effects were on the central nervous system and not the muscles in the body (Lipman, 2010). Meprobamate rapidly gained wide acceptance within the medical community, and in 1957 one-third of all prescriptions written in the United States were for this compound (Lipman, 2010). This compound's chemical structure is very similar to that of the barbiturate, but just different enough so that the claim that it is not a barbiturate is justified.

Shortly after it was introduced, it was discovered that it could also induce a sense of euphoria when misused at high dosage levels (Bisaga, 2008). However, like its “non-addicting” counterparts, it was soon discovered that there was a significant addiction potential associated with its use. Physical dependence on meprobamate is common when patients require 3,200 mg/day to achieve the desired effects (Cole & Yonkers, 1995). By current standards it is considered obsolete, and is very rarely prescribed today. Surprisingly, an over-the-counter prodrug, **carisoprodol**, is biotransformed in part into meprobamate after ingestion, and there have been reports of physical dependence on carisoprodol (Bisaga, 2008; Gitlow, 2007).

Peak blood levels of meprobamate are seen in 1–3 hours after a single dose, and the half-life is between 6 and 17 hours, although when used on an extended basis the half-life might be extended to between 24 and 48 hours (Cole & Yonkers, 1995). The lethal dose of meprobamate is estimated to be about 28,000 mg; however, some patients have expired after ingesting only 12,000 mg (Cole & Yonkers, 1995). When combined with other CNS depressants, the therapeutic

window for meprobamate is reduced and multidrug fatal overdoses were not uncommon.

Methaqualone (often known as quaaludes) was introduced as a safe, “nonaddicting” barbiturate substitute in 1965, and it quickly gained a following among those who use illicit drugs, who discovered that if you resisted the hypnotic effects of this compound, you were able to induce a feeling of euphoria (Hammer et al., 2015; Neubauer, 2005). Following oral administration, methaqualone is rapidly absorbed from the gastrointestinal tract, and the effects begin in 15–20 minutes. Anxiolytic doses were usually about 75 mg, while hypnotic doses were between 150 and 300 mg. Tolerance to the sedative and hypnotic effects of methaqualone develop rapidly, usually after 2–4 weeks of continuous use (Virani et al., 2012). Unfortunately, after the development of tolerance, many individuals would increase their dosage levels in an attempt to maintain the initial effect, ignoring the fact that methaqualone has a narrow therapeutic window and that the lethal dose remains the same in spite of possible tolerance to the drug's effects. In the United States, methaqualone is a Schedule I⁹ compound and was withdrawn from the market. It is, however, still manufactured in other countries, or manufactured in illicit markets, and so those working in the field of addiction should have at least a working knowledge of its effects.

Alcohol Use and the *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition)

The classification of barbiturate use disorders as presented in the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (American Psychiatric Association, 2013) will be discussed in the next chapter. This is consistent with the inclusion of the barbiturates in the category of a sedative, hypnotic, or anxiolytic compound used in the *DSM-5*.

Chapter Summary

The twin problems of anxiety and insomnia have plagued humans for thousands of years. For much of that time, alcohol was one of the few compounds that were even marginally effective in relieving either disorder, although tolerance to the anxiolytic and hypnotic effects of alcohol develops rapidly when it is used on a continuous basis. The chemical revolution that began in the 1800s, which spawned the

⁹See Appendix 3.

pharmacological revolution in its turn, resulted in the development of a number of compounds with anxiolytic and/or hypnotic effects, although each also had serious side effects that limited its use. In the early 1900s, the first of a new family of compounds, the barbiturates, were introduced. These chemicals were in use for decades before it was discovered that they had a mechanism of action very similar to that of alcohol. It was, however, quickly discovered that cross-tolerance between alcohol and the barbiturates was possible, and that they had a high misuse potential.

Following World War II, a number of new compounds were introduced as safe, nonaddicting replacements for the barbiturates. However, it was soon discovered that each of these compounds also had misuse potential similar to that of the barbiturates. Since the introduction of the benzodiazepines (discussed in the next chapter), most of these compounds have fallen into disfavor. However, a small number of the barbiturates have a limited role in medicine even today, and the health care professional will occasionally encounter a patient who misuses these compounds.

Misuse of the Benzodiazepines and Similar Agents

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 7.1 Understand the history of benzodiazepines
- 7.2 Understand the pharmacology, subjective effects, and complications of benzodiazepines at appropriate prescribed levels
- 7.3 Contrast the pharmacology, subjective effects, and complications of above-normal use of benzodiazepines with normal prescribed levels of use
- 7.4 Describe neuroadaptation to benzodiazepines
- 7.5 Describe the benzodiazepine receptor antagonists
- 7.6 Understand the DSM criteria for sedative, hypnotic, or anxiolytic-related disorders

Introduction

In 1960, the first of a new class of anti-anxiety compounds, chlordiazepoxide, was introduced in the United States. The benzodiazepines (BZs) were identified as a result of the search for safe replacements for the barbiturates, and with their introduction physicians now had a safer alternative to the more dangerous, indeed potentially lethal, barbiturates (Cloos, 2010a; Mihic & Harris, 2011). Since the time of their introduction, more than 3,000 different variations of the core benzodiazepine molecule have been identified. Approximately 35 BZs or BZ derivatives are known, and several are used as pharmaceuticals in the United States and internationally (Soyka, 2017). The BZs have been found to be useful either as the primary treatment or as an adjunct to the treatment of a wide range of disorders, including anxiety states, insomnia, muscle spasms, and the emergency control of seizures (Bisaga & Mariani, 2015). They are popular medications, as the most often prescribed psychotropics (Bisaga & Mariani, 2015). Each year, between 10 and 15% of the adults in the Western world will use a benzodiazepine¹ at least once (Dubovsky, 2005; Fenton, Keyes, Martins, & Hasin, 2010; Gitlow, 2007; Jenkins, 2007). These medications are also frequently misused, either alone or in combination with other drugs. In this chapter, we will review the history, current uses, pharmacology, and some of the ways that these medications are misused.

¹These compounds are classified as Schedule IV drugs. See Appendix 3.

Scope of Prescribed Benzodiazepine Use

Olfson, King, and Schoenbaum (2015) suggested that in 2008² 5.2% of adults in the United States used a benzodiazepine. The percentage of each age cohort who received a benzodiazepine prescription increased with age, as 2.6% of adults in the 18–35-year-old age group received a prescribed benzodiazepine, 5.4% of individuals in the 36–50 age cohort, 7.4% of those in the 51–64 age group, and 8.7% of those in the 65–80 age cohort (Olfson et al., 2015). There has been a trend for psychiatrists to prescribe fewer benzodiazepines than general practitioners (Olfson et al., 2015; Schatzberg & DeBattista, 2015), possibly because prescribed benzodiazepines are a recognized risk factor for falls (especially in older individuals) and the fact that they are no longer accepted as frontline anxiolytics. Approximately 0.7% of individuals over the age of 12 in the United States are thought to misuse benzodiazepines (SAMHSA, 2017).

Medical Uses of the Benzodiazepines

The BZs were introduced with great fanfare as being both safe and nonaddicting,³ offering physicians an alternative to the more dangerous barbiturates then in use. Their relatively large therapeutic windows made physicians feel more comfortable prescribing them for individuals with anxiety symptoms. Since then, the selective serotonin reuptake Inhibitors (SSRIs) have been found to provide long-term anxiety control without the risk of physical dependence inherent in the use of the BZs over extended periods of time, and have to some degree supplemented the benzodiazepines in this role. Still, the BZs have a limited role in medicine, being used to control *acute* anxiety (anxiety attacks, or short-term anxiety from a specific time-limited stressor), and they continue to have a role in the treatment of such conditions as generalized anxiety disorder (GAD) (Baldwin et al., 2013; Stevens & Pollack, 2005).

Some benzodiazepines currently used in the United States, such as diazepam, have been found to be of value in such problems as emergency seizure control in adults (Matthew & Perry, 2016) and children (Chamberlain et al., 2014), as well as for muscle spasms (Lo & Kaye, 2015). The benzodiazepine alprazolam is frequently used as an adjunct to the treatment of depression, and clonazepam has been found

to be effective in long-term control of anxiety (Schatzberg & DeBattista, 2015) and is frequently used in this capacity after other treatments have failed (Raj & Sheehan, 2004; Sadock, Sadock, & Ruiz, 2015). This is only a limited discussion, and the benzodiazepines are used for a variety of other indications beyond just anxiety. In addition, the benzodiazepines were often used as hypnotic agents in the latter part of the 20th century. This is consistent with Lehne's (2013) observation that many central nervous system depressants function as anxiolytics at low doses and as hypnotics at higher doses. Compounds such as flurazepam, quazepam, triazolam, and temazepam were introduced as hypnotic agents in this country. However, since the introduction of a new class of medications known as **benzodiazepine receptor agonists** (alternately called *Z-compounds*, or *BRAs*⁴), the benzodiazepines have fallen into disfavor as hypnotics. The BRAs are more selective than the BZs, and are thought to have a lower misuse potential than the BZs ("Insomnia in later life," 2006). These medications will be discussed later in this chapter.

The Pharmacology of the Benzodiazepines

The various benzodiazepines all have only minor variations in chemical structure, variations mainly affecting their duration of action (Dubovsky, 2005; Sadock et al., 2015). The relative potency and brand names of some of the benzodiazepines currently in use in the United States are reviewed in Table 7-1:

TABLE 7-1 Commonly prescribed benzodiazepines

Generic Name	Equipotent Dose	Brand Name
Alprazolam	0.5 mg	Xanax®
Chlordiazepoxide	25 mg	Librium®
Clonazepam	0.25 mg	Klonopin®
Clorazepate	7.5 mg	Tranxene®
Diazepam	5 mg	Valium®
Flurazepam	15 mg	Dalmane®
Lorazepam	1 mg	Ativan®
Temazepam	15 mg	Restoril®
Triazolam	0.125 mg	Halcion®

SOURCES: Based on Schuckit (2006a); Brunton, Parker, Blumenthal, and Buxton (2008); Mihic and Harris (2011); Sadock et al. (2015); Schatzberg and DeBattista (2015).

²The last full year for which data was available to the researchers.

³However, even the pharmaceutical companies admitted that they were "habit forming," a term that was less likely to make the user anxious about their use than the more accurate term "addictive."

⁴The term BRAs, or benzodiazepine receptor agonists, will be used in this text.

Like many pharmaceuticals, it is possible to classify the BZs on the basis of their pharmacological characteristics (such as degree of lipid solubility, protein binding, etc.). After ingestion, those BZs that are most lipid-soluble will pass from the gastrointestinal tract into the circulation more rapidly than those that are not as lipid-soluble (Ciraulo et al., 2005; Raj & Sheehan, 2004; Sadock et al., 2015). They are also classified based on their chemical structure as (1) 2-keto, (2) 3-hydroxy, or (3) triazolo (Schatzberg & DeBattista, 2015). Another classification system for the BZs is based on their therapeutic half-lives:⁵ (1) ultra-short-acting (<4 hours), (2) short-acting (<6 hours), (3) intermediate-duration (6–24 hours), and (4) long-lasting (24+ hours) (Mihic & Harris, 2011).

Once in the circulation, the benzodiazepine molecules bind to plasma proteins in the blood (Sadock et al., 2015). Between 70 and 99% of the benzodiazepine molecules, or their active metabolites, bind to plasma proteins, although the degree of binding varies from one benzodiazepine to the next (Sadock et al., 2015). Diazepam is more than 99% binding, while only 80% of the benzodiazepine alprazolam molecules bind, for example (Mihic & Harris, 2011). Lipid solubility and distribution pattern of specific BZs are factors that influence the therapeutic effects of that compound on the body, rather than the half-life (Raj & Sheehan, 2004; Sadock et al., 2015). Some of the BZs are sequestered in body tissues such as body fat, and are then slowly released back into the general circulation over extended periods of time, allowing the compound to have an extended half-life (Sadock et al., 2015). Age is one factor that must be considered when a benzodiazepine is prescribed. The bodies of older individuals require longer periods to biotransform and eliminate a benzodiazepine. If a benzodiazepine is required for an older patient, the physician will often prescribe a compound with a shorter half-life, such as lorazepam, or oxazepam, compounds that do not require extensive biotransformation prior to elimination (Olfson et al., 2015).

Lipid solubility determines how rapidly the unbound molecules of a specific benzodiazepine might pass through the **blood-brain barrier** into the brain, where the primary site of action is the gamma aminobutyric acid (GABA_A) receptor site in various regions of the brain (Bisaga, 2008; Bisaga & Mariani, 2015; Raj & Sheehan, 2004). However, researchers have identified more than 20 subtypes of the GABA receptor site, and the role of each in human behavior is still being explored. The chemical structures of many benzodiazepines make the absorption of those compounds very

erratic when they are injected into muscle tissue, and thus they are not usually used in intramuscular injections and are usually administered orally. One exception to this rule is when the patient is experiencing a seizure. In such cases, intravenous injections of diazepam, or a similar benzodiazepine, can aid in seizure control.⁶ Another exception to the rule is midazolam, which is sold under the brand name of Versed®, which is used as a presurgical anesthetic or for procedures that require “conscious sedation.”

Many benzodiazepines require biotransformation before they can be eliminated from the body. In the process of biotransformation, some benzodiazepines produce metabolites that are themselves biologically active. Thus, the *duration of effect* for many BZs might be different from the elimination half-life of the same compound (Dubovsky, 2005; Sadock et al., 2015). An excellent example of this is the benzodiazepine flurazepam, which will produce additional metabolites during the process of biotransformation. Each of these metabolites has its own biological effect on the user. Because of normal variation in the speed at which a given individual's body can biotransform and eliminate flurazepam and its metabolites, a single dose might continue to have an effect on the user for 47–100 hours after a single dose⁷ (Mihic & Harris, 2011). Fortunately, there are benzodiazepines such as lorazepam and oxazepam that either are eliminated unchanged from the body or produce metabolites that have minimal biological effect, making them ideal for some persons.

Although the benzodiazepines are often compared with the barbiturates, the mechanism of action of the BZs is more specific than that of the barbiturates, which is one factor that contributes to their large therapeutic index (Griffin, Kaye, Rivera Bueno, & Kaye, 2013). The benzodiazepine molecules bind at the gated chloride channel activated by GABA but require that GABA molecules be present before they affect neural activity. In contrast, the barbiturates activate this ion channel even in the absence of GABA (Bisaga, 2008; Bisaga & Mariani, 2015; Brunton et al., 2008; Mihic & Harris, 2011). Thus, the benzodiazepines enhance the effects of GABA, forcing the chloride channel to remain open far longer than normal and reducing the firing rate of that neuron (Brust, 2004; Raj & Sheehan, 2004; Ramadan, Werder, & Preskorn, 2006; Sadock et al., 2015).

⁶Many benzodiazepines packaged for intravenous use are diluted in a compound known as propylene glycol, which is toxic to the body. The toxicity of propylene glycol is additive, and prolonged intravenous administration can result in such problems as cardiac arrhythmias, tissue necrosis, hypotension, seizures, and multiple organ failures (Maldonado, 2010).

⁷Earlier editions reported an estimate of up to 280 hours, but researchers have revised that downward to 47–100 hours (Mihic & Harris, 2011).

⁵Remember: There is the *therapeutic* half-life, the *distribution* half-life, and the *elimination* half-life.

Surprisingly, although the BZs have been used for more than a half century as anxiolytic medications, there is strong disagreement regarding long-term use as anxiolytics (Baldwin et al., 2013; Cloos, 2010b; Schatzberg & DeBattista, 2015). Some researchers believe that the BZs are fully effective for only for 1–2 months, after which they become less effective (Ayd, Janicak, David, & Preskor, 1996; Baldwin et al., 2013; Berry & Mugford, 2007; Fricchione, 2004; Whitaker, 2010). It is for this reason that many neuropharmacologists suggested that benzodiazepines be used concurrently with SSRIs for long-term anxiolytic purposes, with the former class of drugs slowly being discontinued after 6–8 weeks (Fricchione, 2004; Raj & Sheehan, 2004; Schatzberg & DeBattista, 2015). This treatment protocol avoids the danger of BZ withdrawal “rebound” anxiety, or the “plateau effect” seen when the prescribed BZ becomes less effective as an anxiolytic over time. Other pharmacologists believe that the BZs are effective for the control of anxiety even over extended periods of time. They maintain that there is little evidence to suggest that persons become tolerant to the anti-anxiety effects of the BZs, although they do seem to reach a plateau, after which the patient will often report that it “just doesn’t work like it used to” (Ciraulo et al., 2005; Raj & Sheehan, 2004). In this case, a dosage adjustment might be called for, although Raj and Sheehan (2004) warn that the patient might be seeking the initial sense of relaxation achieved when the medication was first started. Thus, even within the medical community there is disagreement as to the optimal use of the benzodiazepines, and, as we will discuss later in this chapter, their potential for misuse.

Subjective Effects of Benzodiazepines at Normal Dosage Levels

When initially used as an anxiolytic at normal dosage levels, patients report a reduction in anxiety and a sense of gentle relaxation. Some individuals report a disturbing sense of dissociation, or sometimes amnesia. Very few persons report a sense of euphoria at therapeutic dosage levels. When used as a hypnotic, the BZs initially reduce **sleep latency**,⁸ and, upon awakening, the individual reports having experienced a deep, restful period of sleep.

Benzodiazepines and Suicide Attempts

An ever-present danger when treating depressed persons is that the person will attempt to commit suicide. Because of

their higher **therapeutic index**⁹ the BZs have traditionally been viewed as far safer to use with depressed persons than were the barbiturates. Although they do appear to be *safer* to use with persons who are potentially suicidal as compared to barbiturates, this does not mean they are necessarily *safe* for these individuals. Benzodiazepines are involved in one-third of prescription drug deaths (Webster et al., 2011). Reviews of the research indicate that BZs do increase the risk of suicidal behavior or completion (Dodds, 2017), and combining BZs with opiates or alcohol increases the risk (SAMHSA, 2014). Specifically, alprazolam was found to be one of the compounds most commonly involved in causes of drug-induced death in Florida during the period from 2003 to 2009 (“Drug overdose deaths—Florida, 2003–2009,” 2011). Chronic use of benzodiazepines in combination with significant work stress for physicians has also been shown to impact suicidal behavior (Iannelli et al., 2014). There have also been rare reports of benzodiazepine-induced suicidal thinking in persons who previously had not demonstrated such thoughts (Breggin, 2008), as well as self-harm behaviors during BZ withdrawal (Neale & Smith, 2007).

When used in isolation, the benzodiazepines are relatively nontoxic compounds, with a very large therapeutic window in most cases. However, simultaneously ingesting another CNS depressant (such as alcohol, narcotic analgesics, etc.) the margin of safety is significantly reduced (Breggin, 2008; Cloos, 2010a). Jones, Mack, and Paulozzi (2013) reported, for example, that at least 77% of persons who died while taking a benzodiazepine were also using either a prescribed narcotic analgesic or nonprescribed opiates.¹⁰ If a person is suspected of having developed a drug overdose, that person *should immediately be assessed and treated by medical professionals*.

Chemists have developed a benzodiazepine antagonist called flumazenil, which binds at and blocks the BZ receptor sites. Unfortunately, it is only effective for 20–45 minutes and is specific to benzodiazepines (Brust, 2007b; O’Brien, 2011). A greater problem is that the sudden blockage of the receptor sites normally occupied by benzodiazepine molecules can initiate sudden withdrawal if the individual is a long-term benzodiazepine user. Additionally, irregular heartbeats and seizures are serious risks in utilizing flumazenil (Penninga, Graudal, Ladekarl, & Jürgens, 2016). As discussed elsewhere

⁹Discussed in Chapter 3.

¹⁰Their study was based on an examination of the death certificates issued by county coroners in 2010. The authors noted that in 25% of cases where a drug overdose was identified as the cause of death, the specific drug(s) were not identified, so there is a chance that the proportion of drug overdose deaths involving benzodiazepines and narcotics could be higher than the 77% figure that the authors offered.

⁸See Glossary.

in this chapter, benzodiazepine withdrawal can induce seizures on its own and is potentially life-threatening (Traub, 2009). Thus, flumazenil is of value only in acute overdose situations with persons who have limited histories of benzodiazepine misuse or addiction, and recent meta-analytic data supports the careful consideration of use even in such situations (Penninga et al., 2016).

Side Effects of the Benzodiazepines When Used at Normal Dosage Levels

Around 10% of persons will report a moderate to severe level of sedation when they first start taking a prescribed benzodiazepine (Sadock et al., 2015). That effect will often pass in a few days as the user's body becomes tolerant to the effects of these medications (Stevens & Pollack, 2005). However, when used for the control of anxiety, and when used as a hypnotic, persons may experience some degree of ataxia, as well as a clouding of consciousness that has been described as a sense of floating, or detachment from external reality.¹¹ Amnesia is another side effect commonly noted (Bisaga & Mariani, 2015; Lo & Kaye, 2015). All of these side effects are compounded if the patient is using other central nervous system depressants, including over-the-counter medications such as antihistamines or alcohol (Sadock et al., 2015).

Other side effects of the benzodiazepines when these medications are used at normal dosage levels include irritability, hostility, paradoxical rage, or aggression (Breggin, 2008; Brust, 2004; Drummer & Odell, 2001; Lipman, 2010; Virani, Bezchlibnyk-Butler, Jeffries, & Procyshyn, 2012). The aggression or rage response appears to reflect the benzodiazepine-induced cortical disinhibition effect, similar to that seen in individuals who misuse alcohol. Because both alcohol and the benzodiazepines affect the same calcium channel in the neural wall through the action of each chemical on the GABA molecule, cross-tolerance between alcohol and the BZs is common, and the concurrent use of both compounds is not recommended (Mueser, Noordsy, Drake, & Fox Smith, 2015; O'Brien, 2006).

¹¹Individuals who have been exposed to a traumatic stressor, and thus are at risk for the development of posttraumatic stress disorder (PTSD), have been found not to benefit from benzodiazepine intervention, possibly because the dissociative effect of this class of medications contributes to feelings of not being in control, which is one of the factors that contributes to the development of PTSD (Cloos, 2010a; Shalev, 2009).

It has been found that even when used as prescribed, individuals were 50% more likely to develop pneumonia and faced a higher risk of death from this disorder (Nakafero, Sanders, Nguyen-Van-Tam, & Myles, 2016). In the time since this class of medications was introduced, it has been discovered that at least some benzodiazepines increase the individual's vulnerability to infection and mortality from infection, although the causal mechanism is not clear at this time (Obiora, Hubbard, Sanders, & Myles, 2012). In addition, the BZs have been found to interfere with normal sexual function in both men and women (Clayton, Alkis, Parikh, & Votta, 2016; Finger, Lund, & Slagle, 1997). The BZs have been found to interfere with normal sleep patterns even when used at normal dosage levels (Qureshi & Lee-Chiong, 2004). Further, when discontinued, the BZs have been found to sometimes cause a phenomenon called **rebound insomnia**, forcing the individual to endure episodes of insomnia until the body adapts to the absence of the BZs (Cloos, 2010a; Doghramji, 2003; Qureshi & Lee-Chiong, 2004; Wright et al., 2015). This may result in the patient starting to take the BZ again in an effort to sleep again (Gitlow, 2007).

Even when used at normal dosage levels, the BZs can interfere with normal memory function, a condition called **anterograde amnesia**. This condition, most commonly seen in older persons, is so common that 10% of persons assessed for a memory problem are thought to experience a degree of benzodiazepine-induced memory impairment (Curran et al., 2003; Lehne, 2013). This is one of the reasons why the BZs are not recommended for use with elderly patients. The mechanism for BZ-induced memory impairment appears to be similar to that of the alcohol-related "blackout," and it will last for the duration of the BZ's effects on the user (Drummer & Odell, 2001). The mechanism has been compared with that of Korsakoff's syndrome in that the same regions of the brain are involved in each condition (Ghoneim, 2004a).

Recently Tihihonen, Mittendorfer-Rutz, Torniainen, Alexanderson, and Tanskanen (2015) examined the histories of 21,500 individuals diagnosed with schizophrenia who lived in Sweden. The researchers found that those individuals with schizophrenia who had received large doses of benzodiazepines (>5 mg/day of diazepam or the equivalent of another benzodiazepine) for an extended period of time had a 4.8 times (480%) greater chance of premature death, especially from cardiovascular disease. On the basis of their research, the authors suggested that benzodiazepines not be used for longer than 30 days in persons with schizophrenia. Fontanella and colleagues (2016) conducted a similar study in the United States, examining data on over 18,000 individuals diagnosed

with schizophrenia, finding a greater risk of death by multiple factors, including suicide, for those prescribed benzodiazepines.

Some benzodiazepines require extensive biotransformation before being eliminated from the body. If the patient were to ingest a second or third dose of the medication before the first dose was entirely biotransformed, s/he might begin to accumulate a reservoir of nonmetabolized medication in his/her body that will slowly return to the circulatory system and cause an extended effect on the user's body. A single dose of diazepam might interfere with the individual's ability to drive for up to 7 hours after the dose is ingested, and therapeutic doses of this compound have been shown to prolong the user's reaction time, increasing his/her risk of a motor vehicle accident by 500% (Gitlow, 2007). These medications have also been implicated in the development of a sense of emotional dulling, in which the user finds it difficult to express normal emotions such as grief following the death of a loved one (Breggin, 2008). It has been suggested that Xanax® (alprazolam), a benzodiazepine that has been marketed as an anxiolytic, might have a therapeutic half-life that is so short that the user might suffer early withdrawal symptoms before the next scheduled dose, at least in some users (Bashir & Swartz, 2002; Breggin, 2008). This can result in a situation where the patient starts to take more medication to treat not their anxiety, but the withdrawal symptoms from their last dose as it begins to wear off.

Neurocognitive Impairment

The benzodiazepines reduce the level of neural function in virtually every region of the brain to some degree (Breggin, 2008). In their exploration of benzodiazepine use and cognitive function, Gonzalez, Vassileva, and Scott (2009) suggested that there was "compelling evidence" that long-term benzodiazepine use at therapeutic levels can induce "significant and widespread neuropsychological impairments that persist even after many months abstinence" (p. 436). These transient, drug-induced changes in cognition may or may not resolve with abstinence (Lader, 2014; Stewart, 2005). Further long-term use/misuse of a BZ might cause withdrawal-related seizures for up to 2 weeks after the individual's last use of the drug (O'Brien, 2011). More disturbing were the results of a study conducted by Billoti de Gage and colleagues (2012), who found that the odds of developing dementia in persons 65 years or older was 60% higher for individuals taking a benzodiazepine as opposed to persons not taking a BZ. However, Zhang, Zhou, Meranus, Wang, and Kukull (2016) did not find statistically significant results in their similar study.

Neuroadaptation to, Misuse of, and Addiction to the Benzodiazepines

O'Brien (2006, 2011) suggested that individuals who misuse benzodiazepines fall into one of two groups: first, those individuals who misuse these compounds to achieve a sense of euphoria. This subgroup is rather small, as the majority of those who ingest a benzodiazepine do not report experiencing any significant sense of euphoria. However, individuals who misuse BZs intravenously report a greater sense of euphoria than do those who misuse oral BZs (Bisaga, 2008; Bisaga & Mariani, 2015; Brust, 2004). Individuals who wish to achieve a sense of euphoria usually misuse multiple drugs, a fact that reinforces the injunction that these medications should rarely, if ever, be used to treat persons with SUDs (Jones, Knutson, & Haines, 2004; O'Brien, 2006). Individuals who misuse multiple drugs will usually take a benzodiazepine to supplement the effects of their drug(s) of choice, to minimize the effects of drug withdrawal, and only rarely as a source of euphoria.

The second subgroup suggested by O'Brien (2006, 2011) is comprised of individuals who begin to misuse a prescribed BZ by taking more of it or for longer periods than was prescribed. These two groups are not mutually exclusive; however, for the most part, the second group of individuals who use BZs were prescribed benzodiazepines by a physician and became tolerant to the anxiolytic effects of the medications over time. In their attempt to overcome their growing tolerance to the anxiolytic effect of the benzodiazepines, these persons might slowly increase their daily dose of the prescribed BZ to dangerous levels.¹² For example, although 5–10 mg of diazepam two or three times a day might initially cause sedation and relief from anxiety, there have been reports of individuals building their intake level to 1,000 mg/day as their tolerance to the compound develops over time, a dosage level that might prove fatal to the drug-naïve individual (O'Brien, 2006). Unfortunately, individuals who misuse BZs in this manner are rarely motivated to discontinue using benzodiazepines, in spite of their protests to the contrary (Work Group on Substance Use Disorders, 2007).

In contrast to O'Brien's model, Liebreinz and colleagues (2016) examined the patient-perceived reasons why they began to use benzodiazepines prior to starting to misuse this group of medications. The authors interviewed 41 adults who met the DSM-5 criteria for a use disorder regarding benzodiazepines and found that their sample fell into four groups: (1) persons who sought the initial prescription for relief from

¹²Usually by obtaining prescriptions from multiple doctors, different pharmacies, or illicit suppliers, or by buying drugs from internet sources.

such problems as insomnia, anxiety, depression or muscle tension; (2) persons who were seeking relief from the symptoms of alcohol or drug withdrawal; (3) persons who were misusing benzodiazepines to counter the side effects of other drugs; and (4) persons who sought out benzodiazepines for their ability to induce a sense of euphoria. Unfortunately, as tolerance developed to the initial dose of benzodiazepines, the individual increased the daily dosage levels until he or she was misusing this class of medications at high dosage levels.

More than 50 years after the introduction of the first benzodiazepine, data on the optimal duration of treatment with a BZ remains scarce (Cloos, 2010a). Most patients use these medications for less than one month, making it unlikely that they would experience a **discontinuance syndrome**¹³ (Ciraulo & Knapp, 2009). The probability that the user will experience a discontinuation syndrome increases as a result of continual use of a BZ. Thirty percent of those individuals who take benzodiazepines at therapeutic doses for just 8 weeks will experience a discontinuance process upon cessation of BZ use, for example (Virani et al., 2012). This process was confused with the development of tolerance seen in individuals misusing substances, and many health care professionals have mistakenly interpreted it as a sign of benzodiazepine misuse or addiction.

The discontinuance syndrome reflects the ability of the BZs to initiate the process of **neuroadaptation**¹⁴ to these compounds (O'Brien, 2005, 2006). The neurons in the brain adapt to the continual presence of the inhibitory effects of benzodiazepine molecules by making changes in the GABA receptor site responsiveness. If the patient should abruptly discontinue the benzodiazepine, the delicate balance between excitatory and inhibitory neurotransmission is disrupted, inducing a "rebound" or discontinuance syndrome (O'Brien, 2005). Cloos (2010b) recommended that the BZs be used for only 1–3 months except in cases where more conventional treatments have failed to work to minimize the possibility that a discontinuance syndrome will develop. For similar reasons the Royal College of Psychiatrists (2013) in Great Britain recommend that benzodiazepines not be used on a continual basis for more than 4 weeks.

The symptoms of the discontinuance process will vary as a result of (a) the duration that the person had received a BZ, (b) the dose used, (c) the half-life of the medication used, and (d) the individual's expectations. Approximately 44–50% of persons who took a low dose of a prescribed benzodiazepine over extended periods report withdrawal symptoms, some of which were quite distressing to the user

TABLE 7-2 Benzodiazepine discontinuance syndrome symptoms

Abdominal cramps
Agitation (possibly to the point of mania)
Anxiety (often called "rebound" anxiety)
Anorexia
Ataxia
Confusion
Delirium
Depersonalization/derealization
Depression
Dizziness/hypotension
Fatigue or muscle weakness
Formication
Irritability
Insomnia Myoclonus
Nausea/vomiting
Nightmares
Postural hypotension
Seizures (possibly leading to death) Skin sensitivity
Sweating Tremor
Withdrawal psychosis

SOURCES: Table based on Bisaga (2008); Bisaga and Mariana (2015); Cloos (2010a); Lipman (2010); Miller and Adams (2006); O'Brien (2011); Sadock et al. (2015); Smith and Wesson (2004); Virani et al. (2012).

(Bisaga & Mariani, 2015; Perry et al., 2007). Some of the more common symptoms of the benzodiazepine discontinuance syndrome are identified in Table 7-2.

The discontinuance syndrome in long-term BZ users is similar to that seen in the alcohol and barbiturate withdrawal syndromes, and ranges from mild to severe in intensity. In extreme cases, the benzodiazepine discontinuance/withdrawal syndrome has the potential to be life-threatening¹⁵ (Maldonado, 2010; Perry et al., 2007). In such cases, a gradual "taper" may be instituted over a period of 6–12 months to minimize the individual's discomfort and the risk to their life (Bisaga, 2008; Bisaga & Mariani, 2015; Whitaker, 2010). When the individual's daily dosage level reaches 10–25% of their former dose, they might experience "rebound" anxiety, which could be more intense than the original anxiety for which they were placed on the BZ, at least for a few weeks (Wesson & Smith, 2005). The use

¹³See Glossary.

¹⁴See Glossary.

¹⁵It is for this reason that benzodiazepine withdrawal should *only* be attempted under the supervision of a physician trained in working with this discontinuance syndrome.

of mood stabilizers, or Seroquel® (quetiapine fumarate), has been suggested as an anxiolytic if the patient should request help with their anxiety during the taper (Wesson & Smith, 2005), although carbamazepine has also been recommended (Sadock et al., 2015). Further anticipatory guidance might prove of value for persons going through the discontinuance syndrome, so that the patient might understand the symptoms, their cause, and that this is a transitory phase.

A surprising side effect of benzodiazepine use increases the risk of the patient committing a homicide by 45% (Tiihonen, Lehti, et al., 2015). The reason for this is not known, but may reflect the same disinhibition effect seen when a person is drinking, becomes involved in a dispute with another person, and then takes an action that they normally would not do such as grabbing a knife and using it.

Benzodiazepine Misuse

The team of Fenton and colleagues (2010) defined the non-medical use of a medication as (a) use without a prescription, (b) use of a medication in doses higher than prescribed, or (c) use of a medication for reasons other than that prescribed by the physician. Unfortunately, benzodiazepines lend themselves to each category of misuse. Clinical experience has found that individuals who misuse BZs use these compounds (a) to enhance the effects of another drug of misuse, (b) to control some of the unwanted side effects of the primary drug, or (c) to help control the effects of the withdrawal process from their primary drug (Longo, Parran, Johnson, & Kinsey, 2000). Research has found that 80% of those who misuse benzodiazepines also have other substance use disorders and the BZs are not usually the primary drug used (Longo et al., 2000; Sattar & Bhatia, 2003). Benzodiazepines with shorter half-lives such as diazepam, lorazepam, alprazolam, and triazolam have the highest misuse potentials (Ciraulo & Sarid-Segal, 2005; Mueser et al., 2015). However, there is also evidence that clonazepam has gained favor with some individuals who misuse BZs (Dubovsky, 2005; Hernandez & Nelson, 2010; Longo & Johnson, 2000).

An example of how the BZs are used to enhance the effects of other drugs that are misused is found in cases where a person on a methadone maintenance program also uses a BZ to obtain a sense of euphoria when these compounds are intermixed. This might explain why 25–90% of persons in methadone or buprenorphine maintenance programs also use benzodiazepines (Bisaga, 2008; Bisaga & Mariani, 2015; Ciraulo & Knapp, 2009; Peles, Adelson, & Schreiber, 2014). It is not known how many of these individuals *need* a benzodiazepine, as opposed to wanting them because of the interactive effect between the two medications. The exact mechanism for the euphoria reported when both compounds

are used is not known, but may reflect the suppression of cortical inhibitions (Ciraulo et al., 2005), or indirect activation of the mu opioid receptor site (Bisaga, 2008). The usual practice for the patient on a methadone maintenance program is to ingest a massive dose of a benzodiazepine (the equivalent of 100–300 mg of diazepam) between 30 and 120 minutes after ingesting the methadone to “**boost**”¹⁶ its effects and induce euphoria (Lipman, 2010; O’Brien, 2005, 2006).

An example of the second reason for BZ misuse is seen in persons who misuse a central nervous stimulant such as cocaine or the amphetamines and who use benzodiazepines or alcohol to control the unwanted side effects of their primary drug of choice. The third category of benzodiazepine misuse is seen in cases where an individual who is dependent on alcohol wishes to avoid the smell of alcohol on his or her breath during the day, and uses a BZ as a substitute. Benzodiazepine intoxication is very similar to alcohol intoxication, causing slurred speech and ataxia but without a residual alcohol smell on the breath. Another example of the third category of BZ misuse is seen in persons who are heroin dependent and who are going through unsupervised heroin withdrawal. It is not unusual for these individuals to use large doses of a benzodiazepine to eliminate or mitigate their withdrawal distress, something they may learn about through others who have used this method.

Persons who are recovering from *any* SUD are at risk for a reactivation of their addiction if they should receive a prescription for a BZ. For example, approximately 25% of recovering alcoholics relapse after receiving a prescription for a benzodiazepine (Fricchione, 2004; Gitlow, 2007; Sattar & Bhatia, 2003). At best, there is only limited evidence that the BZs can be used safely by persons who have an SUD (Drake, 2007; Sattar & Bhatia, 2003). This is most clearly seen in the results of the study conducted by the team of Clark, Xie, and Brunette (2004), who found that while the BZs are often used as an adjunct to the treatment of various forms of mental illness, their use did not improve clinical outcomes, and that persons with SUDs were likely to try to misuse their BZs. It is for this reason that it is recommended that benzodiazepines be used *only* after alternative treatments have failed in persons with a substance use disorder (Ciraulo & Nace, 2000; Seppala, 2004; Sommer, 2005). Further, if benzodiazepine treatment is necessary, the prescribing physician should put special restrictions in place to limit the patient’s access to large amounts of the medication (Seppala, 2004). The debate continues, as some believe that they should not be used with individuals with SUDs (DuPont, 2017), and others believe they should still be considered, although carefully (Parks, Frone, Muraven, & Boyd, 2017).

¹⁶See Glossary.

Drug Interactions Involving Benzodiazepines

The most popular method of BZ administration is orally, a process that can be significantly slowed if the patient should also take a dose of an over-the-counter antacid (Raj & Sheehan, 2004; Workman & LaCharity, 2016). The concurrent use of cimetidine (Tagamet®) can result in increased benzodiazepine blood levels (Tatro, 2009), and thus these medications should only be used under a physician's supervision. There have been a "few anecdotal case reports" (Ciraulo et al., 2006, p. 267) of persons who had an adverse reaction while taking BZs and lithium. The authors reviewed a single case report of a patient who developed profound hypothermia, which was attributed to this combination of medications. Further, the authors suggested that the combination of lithium and the benzodiazepines diazepam and oxazepam may cause higher levels of depression in persons who intermix these medications.

Persons who are taking disulfiram (Antabuse®) should use benzodiazepines with caution, since the combination of these medications can reduce the speed at which the liver can biotransform benzodiazepines such as diazepam and chlor-diazepoxide (DeVane & Nemeroff, 2002; Tatro, 2009). Research shows that use of lorazepam may be an appropriate choice for those on disulfiram who struggle with anxiety as well (Bogenschutz et al., 2016). Surprisingly, grapefruit juice has been found to slow the process of enzymes involved in biotransformation, slowing the rate at which the benzodiazepines might be biotransformed (Mihic & Harris, 2011; Valdez, Boggs, Boggs, & Rey, 2016). Further, benzodiazepine use can alter the blood levels of many antipsychotic medications such as haloperidol and fluphenazine by competing with the BZ molecules for access to the liver's biotransformation enzymes (Ciraulo et al., 2006).

There is limited evidence to suggest that benzodiazepines may enhance the respiratory depressant effect of buprenorphine if these medications are used concurrently, possibly with lethal results (Ciraulo et al., 2006). Use of alternatives to BZs for anxiety is encouraged when using buprenorphine, given that BZs have not been found to enhance treatment outcomes but do increase the risk for accidental injuries, particularly in females (Schuman-Olivier et al., 2013). Benzodiazepine use has been shown to alter the blood levels of digoxin, and persons receiving both medications should have frequent blood level tests to avoid the danger of drug-induced digoxin toxicity. Persons receiving prescription medications such as phenytoin, mephenteroin, ethotoin, fluoxetine, propranolol, and metoprolol should be aware of the danger that these medications might

interfere with the biotransformation of benzodiazepines such as diazepam (DeVane & Nemeroff, 2002). Persons who are taking the anxiolytic medication alprazolam and who also take St. John's wort might experience *more* anxiety than usual, as the latter compound induces a more rapid biotransformation of alprazolam, thus limiting its anxiolytic effects (DeVane & Nemeroff, 2002; Valdez et al., 2016).

Because of the potential for a synergistic effect between the two medications, persons taking *any* form of CNS depressant medication should not take a BZ except under the supervision of their physician. The effects of two or more CNS depressants might result in higher than anticipated levels of sedation to perhaps life-threatening levels of respiratory depression. Persons who use the herbal medicine kava should not use a benzodiazepine, as the former compound will enhance the sedative effects of the benzodiazepine to potentially dangerous levels (Valdez et al., 2016). There have been case reports indicating that the benzodiazepine blood levels in women using hormone-based birth control medications might be lower than normal because the birth control medication increased the speed of benzodiazepine biotransformation (Tatro, 2009).

It is important to note that persons taking valproic acid and lorazepam might become comatose because of the interaction between these two compounds (Wynn, Oesterheld, Cozza, & Armstrong, 2009). While this list does not include every potential interaction between benzodiazepines and other compounds, it should alert the reader to the need for the patient to check with a pharmacist or physician before mixing benzodiazepines with other prescribed, over-the-counter, or herbal compounds.

Long-Term Consequences of Chronic Benzodiazepine Use

The benzodiazepines were originally introduced in the 1960s as safe and nonaddicting substitutes for the barbiturates, to be used both as anxiolytic and hypnotic agents. Surprisingly, the benzodiazepines have been found to be neither safe nor nonaddicting. Health care professionals have learned that they must weigh the potential benefits of the use of benzodiazepines against their potential dangers. Further, although frequently prescribed as anxiolytic agents, their use in the long-term treatment of anxiety continues to be controversial (Salzman & Shader, 2015).

Persons may come to anticipate their next dose of a prescribed BZ to help them cope with what they view as insurmountable anxiety. This is a form of "psychological" dependency that is independent of the process of neuroadaptation. Such persons may engage in "clock watching" as the time nears for their next anticipated dose, and then eagerly

take the dose to avoid what might actually be rebound anxiety induced when the previous dose begins to wear off (Raj & Sheehan, 2004). For example, it is possible to start to experience withdrawal symptoms between doses of alprazolam (Breggin, 2008). To minimize this danger, BZs with longer half-lives have been suggested, which is one reason why clonazepam is gaining popularity as an anxiolytic. The longer half-life of this compound means that blood levels will drop more slowly between doses, controlling rebound anxiety.

Although once widely used as a hypnotic, evidence suggests that the process of neuroadaptation to the hypnotic effects of the benzodiazepines causes them to lose effectiveness after perhaps a week or two of nightly use (Carvey, 1998). It is for this reason that the BZs are recommended only for the *short-term* treatment of insomnia, and only after other potential treatments of insomnia are ruled out (Conroy, Arnedt, & Brower, 2008; Taylor, McCracken, Wilson, & Copeland, 1998). Surprisingly, some patients report having used a BZ as a hypnotic for weeks, months, or even years, suggesting that the process of taking these medications has become part of the psychological ritual that the individual follows to ensure proper sleep more than a pharmacological effect of the BZs (Carvey, 1998).

The BZs do induce a form of sleep, although they interfere with the normal sleep cycle, and suppress rapid eye movement (REM) sleep. If used for extended periods of time, the REM suppression might cause the sleeper to experience **REM rebound**.¹⁷ The patient should be warned that this is a possible reaction to the discontinuance of the benzodiazepine. It has been suggested that therapeutic doses of **melatonin**¹⁸ might also prove useful in promoting normal sleep in the former benzodiazepine user (Garfinkel, Zisapel, Wainstein & Laundon, 1999; Peles et al., 2007; Pettit, 2000).

Section Summary

As should be evident by this point, the benzodiazepines offer the individual a double-edged sword. While they have a number of potent applications, they also have many side effects that make their use problematic at best, if not life-threatening. These compounds may be misused in a number of ways, and individuals may seek them out for their primary effects. More commonly, the benzodiazepines are misused to control or mitigate the effects of the individual's primary drug(s) of choice, to control the symptoms of withdrawal from other compounds, or as a substitute for other compounds that may not be available to the individual at that time. Because of these drawbacks, pharmaceutical companies

have continued the search for compounds that may offer a safer alternative to the benzodiazepines, many of which will be discussed in the next section of this chapter.

The Benzodiazepine Receptor Antagonists (Z-Compounds or BRAs)

Buspirone

BuSpar® (buspirone) was discovered as a result of a search for an antipsychotic compound that lacked the harsh side effects of existing agents; however, its antipsychotic potential was found to be limited. Researchers were impressed by its ability to reduce the individual's anxiety level, and initially thought that it would be as effective as the benzodiazepines as an anxiolytic (Drummer & Odell, 2001). It was introduced as an anxiolytic agent in 1986. Chemically, buspirone is a member of the *azapirone*¹⁹ family of compounds, which differ from the benzodiazepines, and the latter group of pharmaceuticals should not be taken with alcohol.

INDICATIONS FOR USE OF BUSPIRONE

Buspirone is most effective in controlling generalized anxiety disorder (GAD), but does not seem to mitigate the discomfort of the panic attacks that so often accompany GAD (Hudziak & Waterman, 2005; Sadock et al., 2015). In some cases, it does seem to help augment the effects of the selective serotonin reuptake inhibitor class of antidepressants (Egger & Hebert, 2011; Sadock et al., 2015). It was originally thought to function as an antidepressant in its own right, although there is mixed research evidence to support this theory (Egger & Hebert, 2011; Sadock et al., 2015). It is generally not seen as having value in treating the alcohol or benzodiazepine withdrawal syndromes (Hudziak & Waterman, 2005; Sadock et al., 2015). There is limited evidence that it might assist persons who wish to discontinue the use of cigarettes and who experience a degree of anxiety in this process (Egger & Hebert, 2011; Sadock et al., 2015). It may also be helpful in relation to some PTSD symptomology (Sadock et al., 2015). However, it has no significant anticonvulsant potential and its use by persons who have a seizure disorder is not recommended (Schatzberg & DeBattista, 2015; Virani et al., 2012).

THE PHARMACOLOGY OF BUSPIRONE

Buspirone's mechanism of action is not well understood at this time. It does not interact in the same way as

¹⁷See Glossary.

¹⁸See Glossary.

¹⁹The team of Perry et al. (2007) suggested that it was a member of the *azaspirodecandione* family of chemicals.

benzodiazepines on the GABA receptors (Schatzberg & DeBattista, 2015). Presynaptically, it seems to function as a full agonist at the **serotonin**²⁰ 5-HT_{1A} receptor site of the dorsal midbrain raphe, inhibiting the synthesis of serotonin in this region of the brain (Perry et al., 2007). It also appears to function as a partial agonist of the 5-HT_{1A} receptor sites in the limbic region and cortex (Perry et al., 2007; Ramadan et al., 2006; Schatzberg & DeBattista, 2015). It also functions as an agonist and antagonist at the dopamine type 2 receptors (Sadock et al., 2015).

Depending on the individual's biochemistry, peak blood levels of buspirone are achieved in 40–90 minutes following a single oral dose, although the absorption might be doubled if it is taken with food (Perry et al., 2007; Sadock et al., 2015). It is extensively biotransformed during the first-pass metabolism process (Hudziak & Waterman, 2005), and during biotransformation at least seven major and five minor metabolites are produced. Only one of the intermediate metabolites is thought to be biologically active,²¹ and it is hypothesized that this metabolite is the cause of buspirone's adverse effects. In the body, 99% of buspirone becomes lipid-bound, and its elimination half-life is approximately 2.5 hours. This requires the patient to take a dose three times a day, as opposed to just once or twice a day for the long half-life benzodiazepines like clonazepam or diazepam (Sadock et al., 2015). There is no evidence of cross-tolerance between buspirone and alcohol or the benzodiazepines (Sadock et al., 2015). However, persons taking a BZ might have to be tapered off of the original compound before started on buspirone (Perry et al., 2007; Sadock et al., 2015). The misuse potential of buspirone is limited (Smith & Wesson, 2004). There is no evidence of a discontinuance process similar to that seen in benzodiazepines, and no evidence of buspirone-related memory impairment or tolerance to its effects.

ADVERSE EFFECTS OF BUSPIRONE USE

The most serious adverse effect of buspirone use is the development of the **serotonin syndrome**.²² The development of the serotonin syndrome is more common when buspirone is used concurrently with the antidepressant medications bupropion or fluvoxamine, but it can develop under other conditions (Sternbach, 2003). There have been no reported deaths from buspirone overdoses. However, the potential exists that an individual has ingested multiple agents in an overdose and thus *any known or suspected drug overdose must immediately be assessed by a physician* to reduce risk to the individual's life (Perry et al., 2007).

SIDE EFFECTS

Some of the reported side effects of buspirone include headaches, dizziness, drowsiness, nervousness, a sense of disquiet, dysphoria, a degree of psychomotor impairment, excitement, fatigue, **priapism**,²³ nasal congestion, blurred vision, and gastrointestinal upset (Hudziak & Waterman, 2005; Perry et al., 2007; Virani et al., 2012; Workman & LaCharity, 2016). Buspirone has been determined to induce a condition known as *pseudo-Parkinsonism*, and there have been reports that it exacerbates the symptoms of Parkinson's disease (Perry et al., 2007). The safety of this compound during pregnancy has not been determined as of this time.

DRUG INTERACTIONS INVOLVING BUSPIRONE

Buspirone is known to interact with the antidepressant medications known as monoamine oxidase inhibitors (MAO inhibitors, or MAOIs). It is recommended that persons taking these antidepressant medications discontinue them two weeks or more before starting buspirone to avoid drug-induced hypertensive episodes (Ramadan et al., 2006). Persons taking the medications diltiazem, verapamil, erythromycin, itraconazole, or clarithromycin should not take buspirone, as they block its biotransformation and cause buspirone blood levels to rise beyond the recommended level (Ramadan et al., 2006; Venkatakrishnan, Shader & Greenblatt, 2006; Virani et al., 2012). Persons taking this medication should avoid grapefruit juice (Skidmore-Roth, 2016). While this list is not all inclusive, it does demonstrate the need for the patient to consult a psychiatrist before taking buspirone concurrently with any other medication.

Zolpidem

Zolpidem is another member of the BRA class of medications. It was introduced in 1993 and in the United States is sold under the name of Ambien®. This compound belongs to the *imidazopyridine* family of compounds, and is more selective than the benzodiazepines in that it binds at just a subset of the benzodiazepine receptors in the brain. This allows zolpidem to have only a minor anticonvulsant effect, and that is usually seen only at dosage levels above the hypnotic dose (Doble, Martin, & Nutt, 2004). Unlike the benzodiazepines, zolpidem causes only a minor reduction in REM sleep when used at normal dosage levels, and it does not interfere with the normal progression through the stages of sleep, allowing for a more restful night's sleep (Doble et al., 2004; Schuckit, 2006a).

Zolpidem is administered orally, and, after a single dose, peak blood levels are achieved in approximately 1.6 hours (Sadock et al., 2015). The elimination half-life is between

²⁰See Glossary.

²¹Which, if you must know, is 1-pyrimidinylpiperazine.

²²See Glossary.

²³See Glossary.

2 and 3 hours in younger adults, and slightly longer in older adults (Doble et al., 2004; Dubovsky, 2005; Mihic & Harris, 2011; Sadock et al., 2015). Women tend to biotransform zolpidem more slowly than do men, a fact that the manufacturer recognizes, providing the physician with different prescribing recommendations for women and men. For both men and women, the majority of a single dose of zolpidem is biotransformed in the liver into inactive metabolites, which are then excreted by the kidneys. There is some controversy over whether a person might become tolerant to zolpidem's ability to induce sleep. Holm and Goa (2000) suggested that there was little evidence of neuroadaptation to zolpidem's hypnotic effects even after as long as one year of regular use at therapeutic doses. However, Schuckit (2006a, 2006b) disagreed with this assessment, noting that a limited degree of neuroadaptation can develop after the medication has been used for as little as two weeks at therapeutic doses. There have also been rare reports of persons becoming tolerant to its hypnotic effects after using it at very high dosage levels for a number of years (Holm & Goa, 2000). Ultimately, it seems that there may be a mild withdrawal syndrome, lasting between 1 and 4 days, depending on dosage (Sadock et al., 2015).

ADVERSE EFFECTS OF ZOLPIDEM

AT NORMAL DOSAGE LEVELS

The adverse effects of zolpidem appear to be dose-related and it is recommended that the patient be maintained on as low a dose as possible. Some of the side effects reported to date include nightmares, headache, gastrointestinal upset, agitation, some degree of residual drowsiness, dizziness, isolated reports of zolpidem-induced hallucinations or psychotic reactions, "hangover" effects after use, and rebound insomnia when the medication is discontinued (Breggin, 2008; Raza, Kennedy, & Latif, 2014; Sadock et al., 2015; Schuckit, 2006a). Since zolpidem binds to blood proteins, people who struggle with anorexia tend to have higher blood levels of zolpidem because of the reduced number of binding sites available in their blood (Raza et al., 2014).

Although less likely to induce memory impairment than benzodiazepines, zolpidem does cause some cognitive performance problems, and there have been rare reports of sleepwalking phenomena in which the person has engaged in binge eating or other complex behaviors. Like the benzodiazepines, zolpidem can induce states of anterograde amnesia. There have been reports of people engaging in sleepwalking behaviors in which they eat meals, or drive motor vehicles after taking zolpidem without later recalling that they engaged in these activities (Breggin, 2008; Farkas, Unger, & Temple, 2013). There have also been reports of users experiencing suicidal thoughts while taking this medication as prescribed, but for unknown reasons (Breggin, 2008; Ciraulo & Knapp, 2009).

There is also a risk of the user falling. In hospital settings, up to 3% of patients who received a dose of zolpidem experienced a fall, as opposed to less than 1% of those patients who had been prescribed the medication but who did not take it (Kolla, Lovely, Mansukhani, & Morgenthaler, 2012). Such falls increase the individual's risk of additional, potentially fatal injuries. Unfortunately, there is little evidence that other hypnotic medications are substantially safer, thus posing a dilemma for the physician faced with a patient with insomnia (Kolla et al., 2012). Zolpidem is also contraindicated in persons with sleep apnea, as it increases the duration and frequency of apnea episodes (Holm & Goa, 2000).

EFFECTS OF ZOLPIDEM AT ABOVE-NORMAL DOSAGE LEVELS

At dosage levels above 20 mg/day zolpidem has been found to reduce REM sleep time, and there are reports of persons experiencing REM rebound when they discontinue the medication (Ciraulo et al., 2005). Volunteers who ingested 50-mg doses reported such symptoms as visual perceptual disturbances, ataxis, dizziness, nausea, and/or vomiting. Persons who ingested up to 40 times the maximum recommended dosage have recovered without ill effects. There is an apparent synergistic effect between zolpidem and other CNS depressants, and some multiagent overdoses have proven fatal. *For this reason, any known or suspected overdose must immediately be evaluated and treated by a physician.*

THE ABUSE POTENTIAL OF ZOLPIDEM

Since the time of its introduction, evidence has emerged suggesting that its misuse potential might be far higher than was originally thought. Its misuse potential is about the same as that of the benzodiazepines (Mihic & Harris, 2011), and tolerance to its effects does appear possible. Ciraulo and Sarid-Segal (2005) presented a case summary of an individual who increased their daily dose from 5–10 mg/day to over 800 mg/day over time, for example. Like the BZs, zolpidem use might trigger thoughts of returning to active drug use (Jones et al., 2004). On a positive note, the misuse potential of zolpidem appears to be highest only in persons with a prior history of an SUD (Ciraulo & Knapp, 2009; Gitlow, 2007; Holm & Goa, 2000).

In the late 1960s and early 1970s, there were reports of individuals who would ingest the medication methaqualone²⁴ and then resist its effects to achieve a sense of euphoria. Not surprisingly, there are rare reports of persons who will do the same with zolpidem, which means that after more than 50 years of dedicated research, we are right back where we were in the middle of the 20th century: Sedating agents are being misused for their euphoric effects by a small number of individuals.

²⁴Legal production of this medication in the United States was discontinued in the 1970s.

Zaleplon

The compound zaleplon is sold in the United States under the brand name Sonata[®]; it is a member of the *pyrazolopyrimidine* class of pharmaceuticals, and functions as a BRA (“Insomnia in later life,” 2006). Animal research suggests that zaleplon has some sedative and anticonvulsant effects, but in the United States it is only approved for use as a hypnotic (Danjou et al., 1999). Zaleplon is administered orally, in capsules of 5 mg, 10 mg, or 20 mg. In most cases the 10-mg dose is thought to be the most effective, although in persons with low body weight the 5-mg dose might be more appropriate (Danjou et al., 1999).

The strongest effects are observed in the first 4 hours after ingestion, and while it seems to improve sleep latency, there is little evidence that it affects total sleep time at therapeutic doses (Perry et al., 2007). This is consistent with the observed half-life of 1 hour (Doble et al., 2006).²⁵ The liver is the site of zaleplon biotransformation, with about 30% of the dose biotransformed through the first-pass metabolism process, and less than 1% of the dose is eliminated from the body unchanged. The majority of a dose is biotransformed by the liver into less active metabolites, which are eliminated in the feces and urine (Mihic & Harris, 2011).

Zaleplon molecules bind at the same benzodiazepine subtype receptor site used by zolpidem (Mihic & Harris, 2011; Walsh, Pollak, Scharf, Schweitzer, & Vogel, 2000). There is little evidence of a drug hangover effect, but the patient is still advised not to attempt to operate machinery for 4 hours after taking the last dose (Danjou et al., 1999; Doble et al., 2003; Walsh et al., 2000).

ADVERSE EFFECTS OF ZALEPLON

Some of the side effects observed at therapeutic doses include headache, rhinitis, nausea, myalgia, anterograde amnesia, dizziness, depersonalization, drug-induced hangover effects, constipation, dry mouth, gout, bronchitis, asthma attacks, nervousness, depression, ataxia, and paradoxical insomnia. Tolerance to the hypnotic effects of zaleplon develop rapidly, and for this reason this compound is intended only for the *short-term* treatment of insomnia. Patients have reported rebound insomnia after discontinuation, although this is more common when the patient was using higher dosage levels (Dubovsky, 2005). The misuse potential is similar to that of the benzodiazepines, especially triazolam (Smith & Wesson, 2004).

When used at therapeutic doses for more than 2 weeks, zaleplon has been implicated as the cause of problems such as muscle cramps, tremor, vomiting, and on rare occasions

withdrawal seizures. Because of its potential to trigger addictive thinking, the team of Jones and colleagues (2004) do not recommend that it be used in persons with an SUD.

Lunesta[®]

Lunesta[®] (eszopiclone) is not a member of the benzodiazepine family of compounds, but functions as a hypnotic intended for the short-term treatment of insomnia, especially in persons who have trouble falling asleep. There is some dispute about the effectiveness of this compound as a hypnotic; however, it does have misuse potential and should be used with caution in persons with a known history of a substance use disorder. Eszopiclone is sold in 1 mg, 2 mg, or 3 mg tablets, and the usual dose is 2–3 mg shortly before bedtime.

Eszopiclone is hardly a safe medicine: Reported side effects of eszopiclone include hangover effect (daytime drowsiness), feeling dizzy, problems concentrating the day after it was used, anxiety, depression, nausea, stomach pain or loss of appetite the day after it was used, constipation, dry mouth, unusual taste, aggression, agitation, thoughts of self-harm or suicide, skin rash, headache, and both auditory and visual hallucinations. Some users have reported experiencing a headache or enhanced feelings of pain following the use of eszopiclone, and some users have reported a loss of sexual desire while taking this medication. There have also been isolated reports of breast enlargement in men who have used this medication. There have been rare reports of **anaphylaxis**²⁶ in persons taking it.

Amnesia following the ingestion of eszopiclone has been reported in some persons who have used this medication, and the risk of this anterograde amnesia increases with higher doses. There have been reports of persons engaging in such behaviors as driving automobiles or engaging in other complex tasks without conscious memory of having done so the next day.²⁷ Because older persons or individuals with liver damage are sensitive to the effects of eszopiclone, it is recommended that the attending physician use the lowest possible effective dose to reduce the possibility of a drug-induced hangover effect the next day. This medication should be used with caution in persons with a history of sedative misuse or addiction, and there are reports that when misused, eszopiclone can induce subjective effects similar to diazepam. The potential of eszopiclone to induce physical dependence is still not clear, but the potential exists for it to be habit-forming.

The person who is using eszopiclone should not mix it with other central nervous system depressants such as alcohol, benzodiazepines or the antihistamines to avoid a

²⁵Remember: It is generally accepted that it takes five half-life periods to eliminate almost all of a compound from the body, so after 5 hours, virtually all of the drug would have been eliminated from the patient's body, allowing the patient to awaken naturally.

²⁶See Glossary.

²⁷If this should happen, the prescribing physician should be notified immediately.

synergistic effect between the substances being used. Patients should not use eszopiclone with psychotropic medications except under the supervision of a physician to avoid possible interaction problems. There has not been any research into the interactional effects between eszopiclone and any of the drugs of that are typically misused.

Ramelteon

Ramelteon is sold in the United States under the brand name of Rozerem®. It is a novel hypnotic agent that binds at the melatonin receptor (Conroy et al., 2008; Sadock et al., 2015; Winkelman, 2006). By enhancing the effects of melatonin, ramelteon is thought to be able to facilitate the sleep cycle, an advantage for persons with alcohol use disorders since their melatonin levels are usually depleted when they stop drinking and enter the early stages of abstinence.

Ramelteon is administered orally, it is rapidly absorbed through the gastrointestinal tract, and peak blood levels following a single dose are found approximately 45 minutes after the medication is ingested (Neubauer, 2005; Sadock et al., 2015; Winkelman, 2006). But the drug is extensively biotransformed in the first-pass metabolism process, with less than 2% of the dose ingested reacting with the brain (Neubauer, 2005; Sadock et al., 2015; Winkelman, 2006). About 85% of the metabolites are found in the urine (Neubauer, 2005). There is no apparent potentiation effect between ramelteon and the benzodiazepines, and the compound has an elimination half-life of between 1.0 and 2.6 hours (Neubauer, 2005; Sadock et al., 2015). It does not seem to exacerbate sleep breathing problems or chronic obstructive pulmonary disease (COPD). There is a minor potentiation effect between ramelteon and alcohol (Neubauer, 2005). While it would appear to be safe to use in persons with a SUD, the possibility that it will trigger a relapse has not been ruled out as of this time.

Rohypnol

Flunitrazepam, which is sold in other countries under the brand name of Rohypnol®, is a benzodiazepine that is not legally sold in the United States, and for this reason it is discussed in a separate section. It is a Schedule IV compound under the Controlled Substances Act of 1970,²⁸ and possession of or trafficking in flunitrazepam might be punished by up to 20 years in prison in the United States. However, flunitrazepam is used by physicians in other countries as a presurgical medication, muscle relaxant, and as a hypnotic (Gahlinger, 2004; Gwinnell & Adamec, 2006; Palmer & Edmunds, 2003). Some persons who travel abroad might receive

a prescription for this medication when they are outside of the United States, and some is smuggled into this country. It is for these reasons that those who work with individuals who misuse or are addicted to substances should have at least some information about this compound.

Flunitrazepam abuse in the United States first came to the attention of the public during the mid-1990s, when it gained a reputation as a “date rape” drug (Gahlinger, 2004). Its pharmacological characteristics, especially when mixed with alcohol, could induce a state of anterograde amnesia that could last for 8–24 hours, a characteristic that many are reputed to have taken advantage of to facilitate a date rape. To combat this, the manufacturer added a harmless compound that would turn the drink a dark blue if it were to be added to alcohol, thus alerting the drinker that it had been tampered with (Klein & Kramer, 2004; Virani et al., 2012).

Flunitrazepam is estimated to be 10 times as potent as diazepam, and this makes it hard to be detected with standard urine toxicology tests (Gahlinger, 2004; Klein & Kramer, 2004). The manufacturer has provided a free urine drug testing kit to law enforcement officials who suspect that the individual was the victim of a date rape (Palmer & Edmunds, 2003). Flunitrazepam is rarely misused alone but is mixed with other compounds (such as marijuana and alcohol) to enhance their effects (Lehne, 2013). Subjectively, the effects of 2 mg of this drug have been compared with the ingestion of a six-pack of beer (Lehne, 2013). The combination of marijuana and flunitrazepam is said to produce a “floating” sensation. Adolescents have been reported to use flunitrazepam to remain intoxicated in class, while avoiding detection by standard drug urine toxicology test kits (Greydanus & Patel, 2003; Wesson & Smith, 2005).

When used in medical practice, physicians usually prescribe 0.5 to 2 mg of flunitrazepam. Peak blood levels are achieved in between 30 and 120 minutes following a single oral dose (Saum & Inciardi, 1997). Flunitrazepam has an elimination half-life that is significantly longer than its duration of effect, since it is rapidly sequestered in body tissues following absorption. This results in the compound having a therapeutic half-life of 8–10 hours but an elimination half-life of 15–66 hours (Klein & Kramer, 2004; Woods & Winger, 1997). Less than 1% of a dose of flunitrazepam is excreted unchanged. Individuals misusing this substance usually take double the recommended dose, which begins to produce sedation in 20–30 minutes, with the desired results lasting 8–12 hours. Since it is a member of the benzodiazepine family of drugs, the effects are similar to those seen with other BZs in use in this country (Klein & Kramer, 2004). It is capable of causing dependence, and, when discontinued, will cause the characteristic benzodiazepine withdrawal syndrome. Withdrawal after extended periods of use is

²⁸See Appendix 3.

potentially dangerous, and like the other BZs, flunitrazepam can induce withdrawal seizures. For this reason, *flunitrazepam withdrawal should be carried out only under the supervision of a physician*. Although it is a potent compound, it is unlikely to ever be legalized in this country.

Sedative, Hypnotic, or Anxiolytic Use Disorders and the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013) identified five subforms of the sedative, hypnotic, or anxiolytic-related disorders:

- Sedative, hypnotic, or anxiolytic use disorder
- Sedative, hypnotic, or anxiolytic intoxication
- Sedative, hypnotic, or anxiolytic withdrawal
- Other sedative, hypnotic, or anxiolytic-induced disorders
- Unspecified sedative, hypnotic, or anxiolytic-related disorders.

The *sedative, hypnotic, or anxiolytic use disorder* category in *DSM-5* is essentially an addiction to one or more medications in this category. Such medications include (but are not limited to) the barbiturates, BZs, and benzodiazepine-receptor agonists such as zaleplon. The *DSM-5* identifies symptoms suggestive of a sedative, hypnotic, or anxiolytic use disorder, and specifies that the individual must have at least two of the identified symptoms in a 12-month period. Tolerance and withdrawal symptoms are accepted as evidence of a sedative, hypnotic, or anxiolytic use disorder, except in such cases where the person was taking the medication as prescribed under a physician's supervision. Modifiers such as "in early remission" or "in sustained remission" as well as "in a controlled environment" are suggested for use as indicated. A significant level of comorbidity between the use of these agents and the use of tobacco products, illicit drugs, and alcohol is suggested in the *DSM-5*, which at times can make the differential diagnosis for the patient's condition difficult. Finally, substance withdrawal symptoms such as rebound anxiety could further cloud the diagnostic picture, according to the *DSM-5*.

The *intoxication* to a sedative, hypnotic, or anxiolytic appears very similar to alcohol intoxication, except that the individual has not ingested alcohol and the observed symptoms are not attributable to another medical condition (hypoglycemia, for example). The *withdrawal* syndromes induced by the sudden cessation or major dosage reduction for these medications are discussed in this chapter, or in

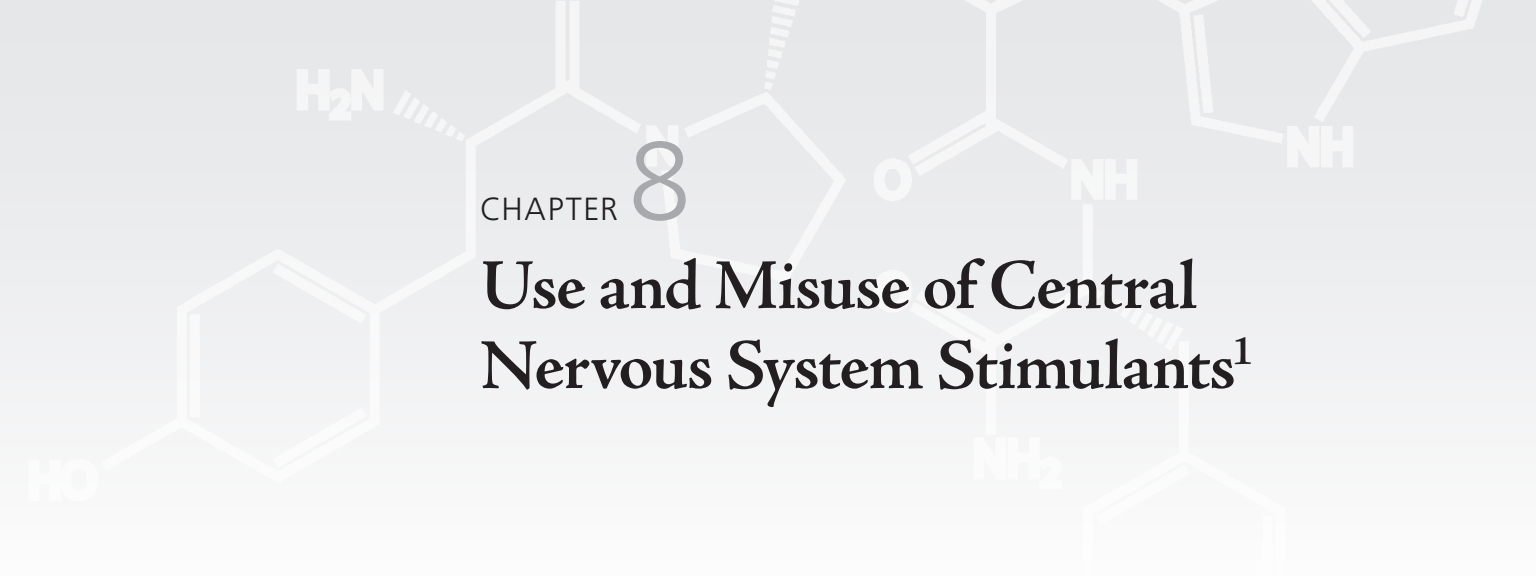
the case of the barbiturates and older drugs, the preceding chapters. Apparently, the *DSM-5* did not differentiate withdrawal from the *discontinuance syndrome* seen when a patient discontinues his or her use of these medications. Individuals may experience a withdrawal syndrome when they discontinue taking any of these medications, and the intensity of these withdrawal symptoms might be life-threatening, making medical supervision of the withdrawal process imperative.

Individuals who warrant a diagnosis of *other sedative, hypnotic, or anxiolytic-induced disorder* demonstrate symptoms of other psychiatric syndromes, the expression of which is either caused, or at least exacerbated, by the misuse of these medications. Such conditions include the various psychotic conditions, states of depression, bipolar, and anxiety. The *unspecified sedative, hypnotic, or anxiolytic-related disorder* category is reserved for those individuals who demonstrate early signs of a sedative, hypnotic, or anxiolytic use disorder but who do not meet the full criteria for this diagnosis.

Chapter Summary

In the middle of the 20th century, pharmaceutical companies began to search for compounds that might be used as anxiolytics and hypnotics, but with a larger therapeutic index than was possible with the barbiturates. In the 1960s, a class of compounds known as the *benzodiazepines* were introduced, and rapidly became the treatment of choice for anxiety control and to help an individual fall asleep. Unfortunately, although they were introduced as "nonaddicting" and "safe" compounds that might be substituted for barbiturates, it is now accepted that they have a misuse potential similar to that of the barbiturates, and they have become a part of the drug misuse problem in the United States.

Pharmaceutical companies have continued the search for safe, nonaddicting compounds that might be used in the control of anxiety and to induce sleep. The first of these non-benzodiazepine compounds were buspirone, introduced in the United States as an anxiolytic, and zolpidem, introduced as a hypnotic compound. Zolpidem is often referred to as a benzodiazepine receptor agonist, or BRA (also called a Z-compound after its chemical structure). The former compound has found only limited applications in the medical field, while the latter has been found to be an effective hypnotic with an abuse potential similar to that of the benzodiazepines. Zaleplon, a BRA, was also introduced as a hypnotic shortly after zolpidem, and also has been found to have an abuse potential similar to the benzodiazepines. There is ongoing research into new compounds that might help treat anxiety and induce sleep controls.



CHAPTER 8

Use and Misuse of Central Nervous System Stimulants¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 8.1** Understand the current medical use of stimulants
- 8.2** Understand the pharmacology and subjective effects of stimulants
- 8.3** Comprehend the current misuse of stimulants, including the methods of use and the effects
- 8.4** Describe the consequences of amphetamine misuse
- 8.5** Understand the DSM criteria for stimulant related disorders

Introduction

Humans have long sought out compounds that would allow them to work harder, work for longer periods of time, fight with more vigor, and as medications to salve the many ills to which we are all heir. This search might have met with at least partial success 60,000 years ago, based on the claims that scientists have found ephedra plants at Neanderthal burial sites in Europe that are thought to date from that era (Karch, 2009; Karch & Drummer, 2016), as well as in northwestern China dating as far back as 40,000 years ago (Xie, Yang, Wang, & Wang, 2013). Historical evidence suggests that Chinese physicians were using the ephedra plant (referred to as *ma huang*) as a medicinal herb to treat respiratory disorders thousands of years before chemists isolated the active agent in the ephedra plant around 1887 (Hill & Weiss, 2011; King & Ellinwood, 2005). This compound was subsequently named ephedrine after the plant from which it was derived (Rasmussen, 2008), and, over the past two centuries, ephedrine has been the center of a long line of central nervous system (CNS) stimulants that have been isolated or developed. All of these compounds are rather controversial, and are the source of much confusion both in the medical community and among the lay public. For this reason, this chapter will be divided into two sections: In the first section the medical uses of the CNS stimulants, including their effects, side effects, and complications from their use will be discussed. In the second section, the complications of CNS stimulant misuse will be reviewed.

¹Since there are no medical applications for khat, the discussion of this compound has been moved to the Chapter 37.

I. CNS Stimulants as Used in Medical Practice

The Amphetamine-Like Drugs

EPHEDRINE

Despite the long history of the plant's use in medicine, and the isolation of ephedrine more than 130 years ago, it remained nothing more than a laboratory curiosity until 1930, when medical journal reports appeared suggesting that ephedrine might be of value for modern medicine for myasthenia gravis (Edgeworth, 1930) as well as asthma (Chen & Schmidt, 1930). Soon a large demand for ephedrine developed, and fears began to develop that the demand might exhaust the available supply. This spurred efforts to find a substitute compound(s) that might be as effective as ephedra, but without the danger of demand exceeding supplies (discussed in "History of the Amphetamines," below).

Medical Uses of Ephedrine

In the past, the medical uses of ephedrine included the treatment of asthma and respiratory problems associated with bronchitis, emphysema, and chronic obstructive pulmonary disease (COPD) (Westfall & Westfall, 2006). Although once considered as a treatment for nasal congestion, it is no longer used for this purpose. In hospitals, ephedrine is used to treat symptoms of shock, and, since it is such a potent vasoconstrictor, some surgical procedures where low blood pressure is a problem (Karch, 2009; Westfall & Westfall, 2006). Ephedrine is still used for some forms of nasal surgery, since it is a vasoconstrictor and thus will limit blood loss when these delicate tissues are injured. It was once used to treat some cardiac conditions, but the advent of newer, more effective medications has made its use in this arena rare (Westfall & Westfall, 2006). However, ephedrine is still used as an adjunct to the treatment of myasthenia gravis and similar syndromes (Vrinten, van der Zwaag, Weinreich, Scholten, & Verschuuren, 2014; Wilson, Shannon, & Shields, 2011).

Pharmacology of Ephedrine

In the human body, ephedrine's primary effects are in the peripheral regions of the body rather than the CNS, with an effect very similar to that of adrenaline (King & Ellinwood, 2005; Westfall & Westfall, 2006). The ephedrine molecule binds at the acetylcholine receptor sites responsible for modulating the constriction or dilation of peripheral blood vessels (Karch & Drummer, 2016; Rothman et al., 2003). When the capillaries constrict, the heart compensates by increasing the force with which it pumps, increasing blood pressure. This makes clinical sense, since ephedrine blocks the reuptake of

norepinephrine² (NE) at the receptor sites used by NE in the regulation of the individual's state of arousal, cardiac response, etc. At the same time, ephedrine is able to cause the smooth muscles surrounding the bronchial passages to relax, improving air flow into and out of the lungs (Westfall & Westfall, 2006).

Depending on the patient's condition, ephedrine might be administered orally or injected via intramuscular or subcutaneous methods. The medication is completely absorbed through all of these methods of administration (Karch, 2009; Westfall & Westfall, 2006). Peak blood levels after a single dose are achieved in between 1 and 3 hours (Drummer & Odell, 2001; Karch & Drummer, 2016). Surprisingly, little is known about the distribution pattern of ephedrine in the body. The half-life is estimated at between 3 and 6 hours (Karch & Drummer, 2016; Samenuk et al., 2002). Virtually all of a single dose is eliminated unchanged, and the amount that is eliminated unchanged depends on the level of acidity in the urine (Karch & Drummer, 2016; Westfall & Westfall, 2006).

Tolerance to the bronchodilation effect of ephedrine develops rapidly, and as a result physicians recommend that the use of ephedrine to treat asthma be limited to short periods of time. Further, the chronic use of ephedrine use can cause or exacerbate cardiac or respiratory problems for the patient, again limiting its use to short periods of time. While marketed as an over-the-counter diet aid, in reality ephedrine appears to have only a modest anorexic effect. The team of Shekelle and colleagues (2003) found in their meta-analysis of the medical literature that ephedrine can help the patient lose 0.9 kg over a short period of time, but there is no data on its long-term effectiveness, nor is there evidence that it will enhance athletic ability, as is commonly believed (Shekelle et al., 2003).

Side Effects of Ephedrine at Normal Dosage Levels

Because the therapeutic index of ephedrine is rather small, it is possible to have toxic effects even at low dosage levels. Even at therapeutic doses, those who use ephedrine are 200–300% more likely to experience autonomic nervous system problems, upper gastrointestinal tract problems, and heart palpitations than nonusers (Shekelle et al., 2003). Although some patients have reported experiencing a sense of euphoria when ephedrine is used at normal dosage levels, patients also have problems such as urinary retention, anxiety or feelings of apprehension, insomnia, headache, hallucinations, tremor, and seizures³ (Samenuk et al., 2002; Zevin & Benowitz, 2007). It was once thought that ephedrine could induce potentially

²A stimulatory neurotransmitter.

³Which technically would make ephedrine an epileptogenic compound for some people, even when used at normal dosage levels.

fatal cardiac arrhythmias when used at normal dosage levels, but there is little evidence to support this belief (Hallas, Bjerrum, Støvring, & Andersen, 2008).

Medication Interactions Involving Ephedrine

It is recommended that patients taking one of the “tricyclic” antidepressants avoid the use of ephedrine, as these medications will enhance the stimulant effect of ephedrine, possibly making the individual quite uncomfortable (DeVane & Nemeroff, 2002). Numerous other potential interactions between medications have been identified, and a pharmacist should be consulted before using ephedrine with another compound.

The Amphetamine Compounds

HISTORY OF THE AMPHETAMINES

The history of the amphetamine compounds is filled with twists and turns worthy of a movie plot. The growing reliance on ephedrine (as discussed earlier in this chapter) to treat respiratory ailments started to raise concern over whether there was a danger of depleting the world’s supply of ephedra plants. Chemists began to search for an artificial substitute for ephedrine to avoid this danger, and since the amphetamine compounds were **analogs**⁴ of ephedrine, they seemed to be the perfect solution to the problem.

The amphetamine compound Benzedrine® was found to have many of the medicinal effects as ephedrine and was soon introduced as a substitute for it (Rasmussen & Keizers, 2016). Benzedrine was sold in a small glass vial with a cap on one end, surrounded by several layers of cloth. This vial initially contained approximately 325 mg of Benzedrine. When needed, the patient would twist the ampule, breaking the glass and releasing the amphetamine compound into the surrounding layers of cloth. Then the patient would inhale the fumes, counteracting the effects of the asthma attack. It was not long, however, before the first reports of amphetamine misuse began to surface (Karch, 2009; King & Ellinwood, 2005; Rasmussen, 2008). Individuals who misused drugs quickly discovered that you could carefully unwrap the cloth, take out the ampule of concentrated Benzedrine, carefully unscrew the cap or break it open at one end, and obtain the concentrated amphetamine contained within for illicit use. It is not clear when the first illicit intravenous injection of Benzedrine took place, but the practice quickly gained widespread acceptance. By the early 1940s, the amount of Benzedrine in each ampule had been reduced by approximately 25% to 250 mg, in part because of the practice of Benzedrine injection. This dose still was the equivalent of 50 of the 5-mg tablets prescribed for

oral use (Rasmussen, 2008). At these dosage levels, the effects were found to be very similar to those of cocaine, which, at the time, was known to be dangerous when misused. The effects of the amphetamines were longer-lasting and thought to be a safe substitute for cocaine, a belief that fueled their misuse.

During World War II, both sides exploited the CNS stimulatory effects of the amphetamines to counteract the effects of fatigue and allow military personnel to work or fight longer. This was done in spite of the limited evidence that it was effective for these purposes, that it was about as effective as caffeine, and that extended periods of use resulted in addiction and visual hallucinations (Rasmussen, 2008). Historical evidence strongly suggests that Adolf Hitler himself was addicted to amphetamines as part of a cocktail of compounds injected into him on a daily basis by his personal physician. Whether this addiction contributed to his ultimate breakdown and the defeat of Germany is open to debate. There were epidemics of amphetamine misuse in Japan and in northern Europe in the years after World War II, when military stores of amphetamine compounds became available.

Medical historians now believe that it was the arrival of large amounts of amphetamine compounds, especially methamphetamine, that contributed to the outbreak of drug-related violence that ended the “Summer of Love” in 1967 (Smith, 1997, 2001). By that time, individuals misusing amphetamines had discovered that high doses of amphetamines could cause agitation and death from cardiovascular collapse. It has also been discovered that following periods of intense amphetamine misuse, the user would enter a depressive state that might last for days or weeks after the last use, possibly reaching suicidal proportions. Although originally believed to be CNS stimulants that lacked the dangers associated with cocaine use, by the mid-1970s, the phrase “speed kills” had been coined as a warning about the dangers of amphetamine misuse (Smith, 1997, 2001). Because of their identified misuse potential and the discovery that the amphetamines had limited effectiveness as pharmaceuticals for any known disease, they were classified as Schedule II⁵ compounds by the Controlled Substances Act of 1970.

CURRENT MEDICAL USES OF THE AMPHETAMINES

The amphetamines might be viewed as compounds in search of a disease that they might treat (Rasmussen, 2008). Because the amphetamines improve the action of smooth muscles in the body, many athletes came to believe that they could improve athletic performance. Subsequent research revealed that the amphetamines have an unpredictable effect on muscle performance, possibly resulting in a *decrease* in athletic performance rather than the desired

⁴See Glossary.

⁵See Appendix 3

improvement. Still, because of the myth that they can improve performance, sports regulatory agencies routinely test for amphetamine compounds, one reason their use by athletes is rather rare.

The amphetamines were found to have an **anorexic**⁶ side effect, and were extensively prescribed by physicians in the 1960s and 1970s for patients who wanted to lose weight. However, research soon demonstrated that tolerance to the anorexic effects of the amphetamines develops rapidly, and that it is not uncommon for patients to then regain the weight they had initially lost. Simple dieting and exercise, behavioral modifications that do not rely on chemicals, were found to result in the same degree of weight loss, and the amphetamines soon lost favor as anorexic agents. However, by this time the amphetamines were being touted as antidepressants. Research has since demonstrated that the antidepressant effects of the amphetamines currently in use are short-lived at best. They are still occasionally used as an *adjunct* to the treatment of depression, because they augment the effects of many antidepressant medications (Hill & Weiss, 2011). Physicians will occasionally exploit the euphoric effect of the amphetamines to counteract depression in the terminally ill, or to counteract the respiratory depression induced by other compounds (Brunton, Parker, Blumenthal, & Buxton, 2007; Fadem, 2009).

Currently, the Food and Drug Administration only approves of the use of amphetamine compounds in the treatment of narcolepsy; “off-label” uses of these compounds include the treatment of some of the effects of AIDS, dysthymia, chronic fatigue syndrome, Parkinson’s disease, the control of anger/aggression in persons with traumatic brain injuries, and lethargy (Karch & Drummer, 2016; Sadock, Sadock, & Ruiz, 2015; Virani, Bezchlibnyk-Butler, Jeffries, & Procyshyn, 2012). Narcolepsy is thought to be the result of a deficit in dopamine levels in certain regions of the brain. Since the amphetamines force neurons to release stores of dopamine, it would appear to be an ideal treatment for narcolepsy and certain forms of depression.

In 1937, it was discovered that the amphetamines had a paradoxical calming effect on children with behavioral problems (Bradley, 1937; Strohl, 2011). Subsequent research revealed that the amphetamines are about as effective in controlling the symptoms of ADHD as is methylphenidate,⁷ calming about 50% of patients with this disorder, and that an addition 25% will experience some degree of improvement when they take prescribed amphetamine compounds (Spencer et al., 2001). This effect is thought to reflect the amphetamine’s ability to enhance the function of the neurons in

the **reticular activating system**⁸ (RAS). However, as is true with methylphenidate, the use of the amphetamines to treat ADHD is controversial. Recent meta-analytic data indicated that there may be significant bias in the studies carried out to date, and that most outcome data showed only low levels of improvement in conjunction with significant side effects (Punja et al., 2016). Although the research reviewed did indicate improvement related to ADHD symptomology, the majority of the studies were less than 6 months in length; thus, further long-term research is needed (Punja et al., 2016). There are those who believe that these compounds may do more harm than good for patients who take them for the control of ADHD (Breggin, 2008; Spencer et al., 2001).

PHARMACOLOGY OF THE AMPHETAMINES

The amphetamines have been in clinical use for almost a century, yet the pharmacokinetics of these compounds have not been studied in detail until recent years (Heal, Smith, Gosden, & Nutt, 2013; Payer & London, 2009). The most common forms of amphetamine are dextroamphetamine (*d*-amphetamine sulfate), methamphetamine, and a combination of dextroamphetamine and pure amphetamine salts (Sadock et al., 2015). Because of its longer half-life, and its ability to rapidly cross the **blood-brain barrier**, individuals who misuse drugs seem to prefer methamphetamine over dextroamphetamine; however, both compounds are misused. The various amphetamines in use have only minor variations in chemical structure that affect the potency and pharmacological characteristics of that compound. The chemical structure of the basic amphetamine molecule is similar to that of the norepinephrine and dopamine molecules, and technically the amphetamines might be classified as an agonist of these compounds (King & Ellinwood, 2007; Lehne, 2013).

When ingested orally, the amphetamine molecule is easily absorbed through the lining of the small intestine, and the usual route of administration in medical practice is orally administered tablets or capsules. On rare occasions, it is administered through intramuscular or intravenous injection in medical practice. In the brain, the effects of any amphetamine are region-specific, causing an increase in neurotransmitter activity in one region while inducing a simultaneous decrease in the release of other neurotransmitters in other regions of the brain (Hanson & Fleckenstein, 2009).

At therapeutic dosage levels, the main effects of the amphetamines appear to be the ability to alter the dopamine neurotransmission system (Fadem, 2009; King & Ellinwood, 2007). The amphetamine molecule causes the release of catecholamine molecules from the presynaptic neurotransmitters, especially dopamine, into the synaptic junction

⁶See Glossary.

⁷Discussed later in this chapter.

⁸See Glossary.

(Fadem, 2009; King & Ellinwood, 2007; Lehne, 2013; Sadock et al., 2015). Then the amphetamines block the reuptake pumps, allowing the dopamine to remain in the synaptic junction longer, enhancing its effects on the downstream neurons. However, they also induce the release and block the reuptake of glutamate, and it is possible that the amphetamine compounds also influence the effects of the acetylcholine neurotransmission system, although this has not been studied in detail (Hanson & Fleckenstein, 2009).

The effects of a single oral dose of an amphetamine begin in about 20–30 minutes, and peak blood levels are achieved in 1–3 hours (Drummer & Odell, 2001). Dextroamphetamine sulfate is an excellent example of this dose-response process, with a rapid rate of absorption, reaching peak effects 1–5 hours after ingestion and a half-life of between 10 and 30 hours (Wilson et al., 2011). The biological half-life of methamphetamine is longer, estimated to be between 6.4 and 15 hours (Cunha-Oliveira, Rego, Carvalho, & Oliveira, 2013). When smoked, the first effects of an amphetamine are seen in 6–8 seconds, and when “snorted” the effects begin about 30–45 minutes after the initiation of use (Gorelick, 2009).

The various forms of amphetamine in clinical use are lipid-soluble; however, because of the limited research into the pharmacokinetics of the amphetamines, it is not known whether one form of amphetamine is more lipid-soluble than any other form of amphetamine. The peripheral effects of the amphetamine compounds are the result of their ability to stimulate the release of norepinephrine (Haney, 2004). There is significant interindividual variability to the effects of the amphetamines. Under normal conditions, 45–70% of a single dose of an amphetamine compound will be excreted unchanged in the urine within 24 hours (Karch, 2009). The exact percentage of the amphetamine that is excreted unchanged depends in large part on the acidity level of the user's blood. The more acidic the individual's blood, the greater the percentage of a given dose that will be excreted unchanged. If the blood is more alkaline, however, then the kidneys tend to reabsorb the amphetamine molecules and return them to the circulatory system. The amphetamine molecules are biotransformed by the liver prior to elimination. Depending on the specific amphetamine ingested, the number of metabolites produced during the biotransformation process will vary. For example, during the process of methamphetamine biotransformation, seven different metabolites are formed before the drug molecules are finally eliminated.

At one point, it was thought that making the patient's urine acidic would speed up the elimination of amphetamine molecules from the circulation, especially if the patient had ingested an overdose (King & Ellinwood, 2005). However, some clinicians believe that this process also increases the patient's chance(s) of developing a cardiac arrhythmia and/

or seizures,⁹ placing the patient's life at risk (Venkatakrishnan, Shader, & Greenblatt, 2006). Thus, it is not clear which course of action the attending physician should follow if the patient should take an overdose of an amphetamine. To complicate matters, there is also a great deal of interindividual variability for toxic reactions to the amphetamines. Some persons have tolerated exceptionally large doses of amphetamines, such as in overdose attempts, without apparent ill effect. Other individuals have been unable to tolerate even low therapeutic doses without experiencing a range of potentially fatal side effects (discussed below). Although amphetamines are classified as central nervous system stimulants, almost 6% of patients taking an amphetamine compound in a clinical trial reported that they felt drowsy and less alert while taking one of these substances (Breggin, 2008). Just under 4% reported feeling confused, and 8.7% reported feeling depressed (Breggin, 2008). Over 17% reported feeling irritable, agitated, and restless, adverse effects that the mainstream media often ignore (Breggin, 2008). These findings illustrate the fact that these compounds are neither perfect nor risk-free.

NEUROADAPTATION TO AMPHETAMINE COMPOUNDS

The steady use of an amphetamine at therapeutic dosage levels will result in an incomplete state of neuroadaptation. When used to treat narcolepsy, the patient might remain on the same dose of the amphetamine for years without any loss of efficacy (Jaffe, Ling, & Rawson, 2005). In contrast, patients develop tolerance to the anorexic effect of amphetamines after only a few weeks, and the drug-induced sense of euphoria does not last beyond the first few doses when amphetamines are used at therapeutic dosage levels. Animal research thus far has shown long-term amphetamine use impacted gene expression of behavioral neuroadaptations into adulthood (Carrey & Wilkinson, 2011).

MEDICATION INTERACTIONS INVOLVING THE AMPHETAMINE COMPOUNDS

Patients who are taking any medication, even an over-the-counter medication, should consult with a physician or pharmacist before starting to take an amphetamine, to avoid the danger of potentially dangerous drug interactions. For example, there is limited evidence that individuals taking any of the **monoamine oxidase inhibitors**¹⁰ (MAO inhibitors, or MAOIs) should not take an amphetamine compound for several days after they discontinue the MAOI in order to avoid potentially lethal hypertensive episodes (Ciraulo,

⁹The amphetamines are epileptogenic compounds, which might cause the individual to experience a seizure, and increasing the chances of a person with a preexisting seizure disorder experiencing a seizure, even if they are fully compliant taking their antiseizure medications (Engel, 2013).

¹⁰See Glossary.

Shader, Greenblatt, & Creelman, 2006). While the potential for these compounds to cause such a hypertensive episode remains unsupported, the danger has not been ruled out, and to avoid this possibility patients should not take these compounds until they have completed an MAOI “wash-out” period of 72 hours or longer.

There is evidence to suggest that amphetamine compounds may interact with at least some of the antipsychotic medications currently in use in the United States (Ciraulo et al., 2006). While this list is hardly exhaustive, it does illustrate that the amphetamines have the potential to interact with other pharmaceuticals in use. A physician or pharmacist should always be consulted about the possible interaction between two different medications if used concurrently.

Subjective Experience of Amphetamine Use in Medical Practice

The subjective effects of an amphetamine administered under a physician's supervision will depend on a number of factors, including the individual's mental state, the manner in which the drug is administered, the relative potency of the dose administered, and the individual's substance use history. For example, a hypothetical soldier who has gone without sleep for 48 hours and who ingests a 5-mg tablet of an amphetamine will have a different reaction than that same soldier would if well rested. The reaction of this hypothetical soldier would be far different still if s/he were to have a 5-mg dose of the amphetamine injected into a vein rather than orally.

Amphetamine compounds do have a very small, virtually insignificant analgesic property of their own, although they may multiply the analgesic effect of a given dose of a narcotic analgesic (King & Ellinwood, 2005). However, amphetamine compounds are rarely if ever used for their analgesic effects, and this property of amphetamine compounds will not be discussed further in this chapter. When used in medical practice, the amphetamines are usually administered orally, in doses of between 5 and 60 mg/day (Jenkins, 2007). At such dosage levels, the user will experience enhanced mood, less mental fatigue, improved ability to concentrate, and perhaps a mild euphoria, especially when the medication is first started (Sadock et al., 2015). The user may also notice that s/he is not hungry as often, and may not feel the need to eat as much as before. As noted earlier, the amphetamines do have an anorexic effect, but only before the development of neuroadaptation to these compounds, after which time the anorexic effect becomes weaker with continued use (King & Ellinwood, 2005).

About 10% of patients started on an amphetamine compound will experience drug-induced tachycardia (Breggin, 1999; Fuller & Sajatovic, 1999). It is for this reason that the physician should conduct tests to rule out preexisting cardiac

problems in the patient before starting the medication. Rarely, patients taking an amphetamine compound at therapeutic doses will develop a drug-induced psychosis (Ciraulo et al., 2006; Lehne, 2013). More commonly encountered are stereotypical, repetitive behaviors, which are especially common when these medications are used at high dosage levels.

Patients with **Tourette's syndrome**¹¹ often find that amphetamine use exacerbates the symptoms of their Tourette's. Some patients begin to engage in the characteristic vocalizations and movements of Tourette's disorder when they begin to take a prescribed amphetamine. Further, although the amphetamines are CNS stimulants, about 40% of patients taking them at therapeutic doses experience a drug-induced feeling of depression that might become so profound as to reach suicidal proportions (Breggin, 1999). When the patient discontinues a prescribed amphetamine, s/he is also prone to experience a depressive reaction, as well as fatigue and lethargy, lasting a few hours or days. These compounds have also been known to interfere with normal growth in children. This information suggests the amphetamines are quite potent compounds, which even at therapeutic doses have the potential to harm the individual.

METHYLPHENIDATE

Methylphenidate has become a rather controversial compound. It was originally introduced in the late 1950s as a safe alternative to the amphetamines, which were then in use as antidepressants. Like the amphetamines, methylphenidate was a drug in search of a disease for many years, being used as an agent to promote weight loss and finally to control the symptoms of attention deficit hyperactivity disorder (ADHD) (Breggin, 2008; Sinha, 2001). Methylphenidate is currently the most-used prescription for ADHD (Zimmer, 2017). There have been strident arguments both for and against the use of methylphenidate in the treatment of ADHD, and it is certain to remain a most controversial compound for many years to come.

Pharmacology of Methylphenidate

This compound has a chemical structure similar to those of the amphetamines and of cocaine (Horstman, 2010), and functions as a CNS stimulant. It was originally developed as a possible nonaddicting substitute for the amphetamines (discussed below) (Diller, 1998). The “habit-forming” potential of the amphetamines had been identified by then, and so it was hoped that methylphenidate could serve as a safer substitute. Some neuropharmacologists classify it as a member of the amphetamine family of drugs. In this text, it will be classified as an amphetamine-like compound.

¹¹See Glossary.

When it is used in the treatment of ADHD, patients are prescribed daily doses of between 15 and 90 mg. Orally administered doses are rapidly absorbed through the gastrointestinal tract (Greenhill, 2006). Peak blood levels are usually achieved around 2 hours following a single dose, although with extended release forms of methylphenidate this might not occur until 4–7 hours after the medication was ingested (Wilson et al., 2011). The estimated therapeutic window of methylphenidate is 1:100, which is to say that the effective dose is approximately 1/100th the estimated lethal dose (Greenhill, 2006). The half-life is between 1 and 3 hours, with the effects lasting 3–6 hours following a single oral dose. These figures are extended in situations where the patient has ingested an extended release form of methylphenidate, and might last for up to 8 hours. About 80% of a single dose is biotransformed into ritanic acid in the intestinal tract, which is then excreted by the kidneys (Karch, 2009).

Within the brain, methylphenidate blocks the action of approximately 50–70% of the molecular dopamine **reuptake pumps**¹² in the neural wall of those neurons that govern wakefulness and concentration (Engel, 2013; Jaffe, Rawson, & Ling, 2005; Volkow & Swanson, 2003; Whitaker, 2010). This allows the dopamine molecules to remain in the synaptic junction longer, thus enhancing their effect. It has also been shown to work in a way similar to norepinephrine (Nevels, Weiss, Killebrew, & Gontkovsky, 2013; Sadock et al., 2015; Zimmer, 2017).

Medical Uses of Methylphenidate

Methylphenidate functions as a CNS stimulant and is of value in the treatment of a rare neurological condition known as **narcolepsy**, ADHD, and is occasionally used as an adjunct in the treatment of depression. On occasion, it is used as an adjunct to the treatment of Parkinson's disease, control of anger/aggression in brain-damaged persons, or AIDS-related neurological problems. There are few, if any, other medical applications of methylphenidate at this time.

Side Effects of Methylphenidate

Methylphenidate's long-term effects have not been studied in depth, since most follow-up studies involving methylphenidate are discontinued after a few weeks. Even studies involving the administration of methylphenidate to animals are usually discontinued after a few weeks or months, in part because of the cost of maintaining the animals over extended periods of time. Although it is reportedly safe at prescribed doses, there is emerging evidence that casts some doubt on this claim (Higgins, 2009). This is a matter of some concern, since there is a growing trend for patients to be told that they must continue taking methylphenidate through childhood into adulthood (Higgins, 2009; Zimmer, 2017).

It was once thought that methylphenidate caused, or at least exacerbated, cardiac problems in users, even at therapeutic doses. In a retrospective study in which the clinical records of 1.2 million children and young adults ages 2–24 who had been placed on methylphenidate or similar compounds for treatment of ADHD symptoms, Cooper and colleagues (2011) failed to find evidence of increased risk of methylphenidate-related cardiac problems. It is possible that children who die while taking methylphenidate as directed had preexisting heart problems that coincidentally caused them to die while taking this medication.

Unfortunately, up to 5% of the children who receive therapeutic doses of methylphenidate will experience visual hallucinations and possibly a medically induced psychosis (Aldhous, 2006; Halevy & Shuper, 2009; Higgins, 2009). Children prescribed methylphenidate have been observed to demonstrate behaviors suggestive of obsessive-compulsive disorder, symptoms that were not present prior to the initiation of this medication (Breggin, 2008). Other identified side effects of therapeutic doses of methylphenidate include anorexia, insomnia, weight loss or failure to gain weight, dry mouth, heart palpitations, angina, anxiety, liver dysfunctions, skin rashes, dizziness, headache, hypertension, exacerbation of Tourette's syndrome, blurred vision, leukopenia, anemia, perseveration, and possible cerebral hemorrhage (Breggin, 2008; Higgins, 2009; Karch, 2009; Newcorn & Ivanov, 2007).

Because of its anorexic side effect, methylphenidate can interfere with normal physical growth (King & Ellinwood, 2005). Animal-based research has revealed that the CNS stimulants (including methylphenidate) can, by increasing the dopamine levels in the brain, interfere with the **pituitary's**¹³ normal function, thus contributing to growth retardation (Higgins, 2009). Patients with a known seizure disorder should not be placed on methylphenidate, as this compound can exacerbate such disorders (Breggin, 1999; Engel, 2013). The mechanism for these seizures is not clear but might reflect drug-induced changes in cerebral blood flow patterns or possibly changes in cellular responsiveness to neurotransmitters that increase or decrease the firing rate of those neurons.

Children who take prescribed doses of methylphenidate frequently report that the drug made them feel like a “zombie” and thus make them resistant to taking it (Breggin, 1999). This appears to be a common effect of methylphenidate (Diller, 1998). However, such reports are disputed. For example, Pliszka (1998) denied that this was a drug-induced effect. Further, a small number of studies have suggested that there is a relationship between methylphenidate use in childhood and possible affective disorders in adulthood (Higgins, 2009). On rare occasions, therapeutic methylphenidate use can also

¹²See Glossary.

¹³See Glossary.

induce a state of depression that may reach suicidal proportions (Breggin, 1999).

There is early research data suggesting a *possible* connection between the use of prescribed doses of methylphenidate and the development of Parkinson's disease later in life (Rothenberger & Banaschewski, 2004). This obviously is a matter of some concern, and further research into possible mechanisms, treatment options, and alternatives is needed in this area. These studies suggest a need for further research into the benefits and long-term consequences of methylphenidate use, even at therapeutic doses.

Medication Interactions Involving Methylphenidate

Patients who are using any of the “tricyclic” antidepressants should not use methylphenidate, as the interaction of these compounds can cause potentially toxic levels of the antidepressant medication to build up in the patient's blood (DeVane & Nemeroff, 2002; Nevels et al., 2013). Patients using any of the MAO inhibitors should not use methylphenidate because of a potential toxic reaction between these compounds (Nevels et al., 2013). Further the use of methylphenidate with the selective serotonin reuptake inhibitor (SSRI) family of antidepressants reportedly can lower the seizure threshold, causing seizures (DeVane & Nemeroff, 2002; Nevels et al., 2013). Finally, patients taking antihypertensive medications might find that their blood pressure control is inadequate, as methylphenidate interferes with the effectiveness of blood pressure medications (DeVane & Nemeroff, 2002). While it is not possible to identify every potential drug interaction involving methylphenidate, this list should highlight the need for the patient to check with a physician or pharmacist before taking methylphenidate with any other medication.

MODAFINIL (PROVIGIL®)

A recent entry into the field of CNS stimulants is modafinil, which is sold under the brand name of Provigil® (Baker, 2009). Provigil was introduced in 1998 as a “wake-promoting agent” (Price, 2009, p. 3), a term that the author suggested was carefully selected to avoid the suspect term “**stimulant**.”¹⁴ It is frequently used to treat narcolepsy. One “**off-label**”¹⁵ use of modafinil is to enhance cognitive endurance for persons suffering from fatigue (Baker, 2009), including fatigue related to cancer and cancer treatment (Hovey et al., 2014; Spathis et al., 2014). Like the other CNS stimulants, modafinil stimulates the release of dopamine within the brain, and as such has a mild misuse potential (Price, 2009; Volkow et al., 2009). For example, it is often misused by those who wish to improve concentration even though they do not have ADHD. In this

capacity, it is often abused by college students who wish to enhance concentration during all-night study sessions. It has also been used in treating cocaine use disorders (Anderson et al., 2009), depression symptoms (Goss, Kaser, Costafreda, Sahakian, & Fu, 2013), and schizophrenia (Minzenberg, Yoon, Cheng, & Carter, 2016).

Pharmacology of Modafinil

The pharmacokinetics of modafinil are not well understood at this time. It does seem to impact norepinephrine reuptake, but evidence does not show the same impact regarding dopamine (Sadock et al., 2015). Following the administration of 2–4 doses (one per day) to establish steady-state plasma levels, the elimination half-life is approximately 15 hours (Thompson, 2011).

Following oral ingestion, the peak blood plasma levels of modafinil are seen in 2–4 hours when ingested on an empty stomach. Although it may be ingested with food, absorption of modafinil will be delayed by approximately 1 hour. Approximately 60% of the drug molecules bind to protein molecules in the blood (mainly albumin). It is biotransformed in the liver, with only 10% of the modafinil being excreted unchanged by the kidneys (Thompson, 2011). This medication is not to be used by patients with a known allergic reaction to this compound (Thompson, 2011).

Side Effects of Modafinil Use

This medication can induce shortness of breath, heart palpitations, chest pain, and transient changes in the electrocardiogram (Thompson, 2011). Its use in patients who have suffered a recent myocardial infarction (heart attack) has not been studied in detail and it should be used in such patients only under a physician's supervision. One patient did develop symptoms of a drug-induced psychosis after taking exceptionally large doses of modafinil, but these symptoms resolved after the medication was discontinued (Thompson, 2011). Other rare reported side effects include hypersexuality (Bulut, Tulaci, Türkoğlu, Bulut, & Orsel, 2015) and cataplexy (Lopes et al., 2014). Modafinil does not appear to induce the sense of CNS over-stimulation seen when a patient receives methylphenidate or an amphetamine compound (Baker, 2009). It does, however, appear to have an addiction potential (“Wakefulness drug: New safety concerns,” 2009).

Medication Interactions Involving Modafinil

This medication is known to reduce the effectiveness of oral contraceptives. Possible interactions with alcohol have not been studied. It is recommended that the patient consult with a pharmacist before taking another medication (including over-the-counter compounds) with modafinil.

STRATTERA® (ATOMOXETINE HYDROCHLORIDE)

Technically, atomoxetine hydrochloride is not classified as a CNS stimulant by the manufacturer, but it is included in

¹⁴A term associated in the minds of many with drugs such as cocaine, etc.

¹⁵See Glossary.

this chapter since, like the other compounds reviewed in this chapter, it is recommended for the treatment of ADHD. It is often preferred over the stimulants, because it has been shown to have a low misuse potential (Upadhyaya et al., 2013).

Pharmacology

Atomoxetine hydrochloride is administered orally, and following absorption approximately 98% becomes protein-bound (Sadock et al., 2015). The exact mechanism of action remains unclear, but it is assumed to be a result of the drug's ability to alter norepinephrine release patterns in the neurons (Sadock et al., 2015). The half-life of this compound is estimated to be approximately 5 hours in the typical patient (Sadock et al., 2015).

Side Effects

Identified side effects include a mild increase in heart rate (approximately 6 beats a minute). Breggin (2008) noted that other reported side effects include irritability, mood swings, and aggressive behaviors by the child receiving this medication. Other reported side effects include grandiosity, hyperactivity, insomnia, and in overdose situations it can induce seizures. The Food and Drug Administration has also required the manufacturer to include a "black box" warning about this compound apparently causing suicidal thinking or suicidal acts in children receiving it (Breggin, 2008).

Medication Interactions

Numerous medication interactions have been identified, and a pharmacist should be consulted before intermixing atomoxetine hydrochloride with other compounds.

Challenges to the Use of CNS Stimulants to Treat Identified Disorders

It has been observed that the amphetamines are "orphan" drugs in search of a disease to treat. Touted first as a treatment for asthma in the 1930s and 1940s, they were then sold as reputed antidepressants in the 1950s, and then in the 1960s as anorexic compounds that could be used to assist in weight loss programs (Breggin, 2008; Rasmussen, 2008). Currently, they are often recommended as a pharmacological treatment for attention deficit disorders and narcolepsy. At the peak of their popularity as pharmaceutical agents in the mid-1960s, fully 5% of the adults in the United States were taking a prescribed amphetamine compound. About half of these patients were misusing amphetamines for their euphoric effects, which underscores the misuse potential of this class of drugs (King & Ellinwood, 2005; Rasmussen, 2008).

Surprisingly, in spite of their use as agents to treat ADHD, there is little evidence of the long-term effectiveness of these compounds for treating such disorders, and a

mounting body of evidence suggesting that psychosocial interventions are far superior (Breggin, 2008; McDonagh & Peterson 2006; Sonuga-Barke et al., 2013), as well as the possibility that diet changes can have an impact on symptomatology as well (Pelsser, Frankena, Toorman, & Pereira, 2017). In spite of this, pharmacological interventions are recommended by physicians and pharmaceutical companies, the latter being more than happy to learn that the diagnosed rate of ADHD might be as high as 9.5% (Visser, Bitsko, Danielson, Perou, & Blumberg, 2010).¹⁶ Obviously, since psychosocial interventions cannot be patented by pharmaceutical companies, they are not mentioned in advertisements for CNS stimulants as treatments for ADHD. Unfortunately, as noted earlier in this chapter, the amphetamine-like drugs have also been identified as possibly causing neural damage even when used as prescribed (Breggin, 2008), raising questions about whether the cure might be worse than the disease states that they are supposed to control.

II. CNS Stimulant Misuse

Scope of the Problem

THE AMPHETAMINES

Shortly after their introduction, the first clinical reports of amphetamine addiction began to appear in the clinical literature, and in response the pharmaceuticals industry quickly settled on the term *habit-forming* as a descriptor for these compounds, to avoid the charge that they were addictive and that users were not being informed of this potential danger (Rasmussen, 2008). Discussion of the problem of amphetamine misuse is complicated by the fact that different researchers define the term "amphetamine" in different ways: Some researchers limit the term to only the compound methamphetamine, while others differentiate between the abuse of methamphetamine and other amphetamine compounds ("meth/amphetamine") (Rutkowski & Maxwell, 2009, p. 6). Some researchers apply the term *amphetamine* only to diverted pharmaceuticals, while others include both diverted and amphetamine compounds produced in illicit "labs" under the rubric of "amphetamine" (Rutkowski & Maxwell, 2009). Finally, some researchers include the hallucinogen MDMA ("Ecstasy") as an amphetamine while others classify it as a hallucinogenic¹⁷ compound.

¹⁶In their defense, it should be noted that the authors of this study spoke about 22% of the children in the survey apparently outgrowing the disorder.

¹⁷The practice that is followed in this book is to classify MDMA, or "Ecstasy," as a hallucinogenic, not an amphetamine compound.

In the United States, the amphetamines, especially methamphetamine, are the second most popular class of illicit drugs, exceeded in popularity only by marijuana. The misuse of prescribed amphetamine compounds is widespread, as evidenced by the fact that 25% of the students at some colleges have used the amphetamine sold under the brand name of Adderall® to help them study for examinations or stay up all night to finish assigned projects (Owen, 2008). Arguably, the stereotypical “**pusher**”¹⁸ for the current generation of young adults is not the seedy man on the street selling little white packets of drugs, but the health care professional in a white lab coat and with a prescription pad (Owen, 2008; Rasmussen, 2008).

Globally, the misuse of the amphetamines or amphetamine-like compounds is thought to be a \$65 billion/year industry (United Nations, 2011). The total number of people who use amphetamines around the globe outnumbers the number of people who use heroin and cocaine *combined* (United Nations, 2016). The mass media in the United States has often spoken about a “meth crisis” in this country, although three-quarters of individuals who use methamphetamine are thought to live in Asia or Southeast Asia (Ling, Rawson, & Shoptaw, 2006), with East and Southeast Asia keeping pace with the United States in the amount of methamphetamine seized by officials (United Nations, 2016). To put the problem of methamphetamine use in the United States into perspective consider the following facts: 44% of people over the age of 12 acknowledge using marijuana at some point in their lifetime, with 17.8% indicating use in the past year; 14.5% acknowledge use of cocaine at some point in their lifetime, with 1.8% using in the past year; and 15.3% indicate use of hallucinogens in their lifetime, with 1.8% using in the past year (SAMHSA, 2016). In contrast, only 5.4% of people over the age of 12 indicate use of methamphetamine in their lifetime, with 0.6% indicating use in the past year (SAMHSA, 2016). While this is not to downplay the dangers associated with methamphetamine use or addiction, it does underscore how the media helps to shape our perception of substance use disorders on a day-to-day basis.

Young adults, or those who are about to become young adults, represent a special risk group for methamphetamine misuse. In a recent survey, 10% of high school seniors admitted to having used an amphetamine compound, 1.2% admitted to the use of methamphetamine at least once, and 1.4% acknowledged use of crystal methamphetamine (Johnston, O'Malley, Miech, Bachman, & Schulenberg, 2017). As these figures demonstrate, the misuse of amphetamine compounds in the United States is both common and widespread.

However, there is still much to be discovered about the epidemiology of amphetamine misuse both in the United States and around the world.

EPHEDRINE

Because it was once sold over the counter as a diet aid and treatment for asthma, the true scope of ephedrine misuse is simply not known (Karch, 2009). It is often sold under the guise of other, more potent, compounds. The side effects of ephedrine misuse include all the side effects noted earlier in this chapter, plus coronary artery vasoconstriction, myocardial infarction, cardiac arrhythmias, stroke, and death (Brust, 2004; Neergaard, 2004; Samenuk et. al., 2002). Ephedrine is also a precursor of the amphetamines, especially methamphetamine, and so restrictions were placed on its access in the United States in 2004. Such restrictions have been found to have minimal effect on methamphetamine production (Cunningham, Liu, & Callaghan, 2009).

METHYLPHENIDATE

There simply is no way to estimate the percentage of methylphenidate pills that is diverted to the illicit drug market, although it is known that it is a popular drug to misuse. There are multiple causes for methylphenidate misuse: Some individuals want to engage in tasks such as driving delivery trucks, or study for exams, for extended periods of time (Vedantam, 2006). Other individuals wish to stay awake at parties longer, or counteract the sedating effects of alcohol so that they can drink longer, while others seek a drug-induced feeling of euphoria (Aldhous, 2006; Arria & Wish, 2006). Such misuse is stimulated by the mistaken belief that this medication is not addicting. A conversion formula suggests that 15 mg of methylphenidate is about as potent as 5 mg of dextroamphetamine (Rasmussen, 2008).

MODAFINIL

The misuse potential of modafinil remains poorly defined, although it is acknowledged that a small percentage of users take the medication to help them remain cognitively alert for longer than normal. It is also increasingly being diverted into the hands of those for whom the drug was not prescribed (Price, 2009). Given the report that it was pharmacologically different from the amphetamine compounds when it was introduced, health care professionals have become complacent about the potential risks associated with modafinil misuse, which is rather frightening because of its growing popularity as a drug to misuse.

ATOMOXETINE HYDROCHLORIDE

No identified pattern of misuse for this medication has been reported as of this time, which is most likely due to its low misuse potential (Upadhyaya et al., 2013).

¹⁸One who sells illicit drugs.

Methods of CNS Stimulant Misuse and Their Effects

EPHEDRINE

Effects of Ephedrine When Misused

The effects of ephedrine misuse are essentially an exaggeration of the adverse effects of ephedrine when used at normal doses.¹⁹ This makes sense, since the user's chances of suffering an adverse effect are dose-dependent. Unfortunately, since ephedrine can induce a feeling of euphoria when used at very high doses, there is an incentive for some people to misuse it. This sense of euphoria is less intense than that seen in those who misuse amphetamines, but it is still experienced when individuals ingest high levels of ephedrine (Erickson, 2007). Further, it is often touted as being a "safer" alternative to synthetic or semisynthetic compounds such as the amphetamines (Gorelick, 2009).

Methods of Ephedrine Misuse

The most common method of ephedrine misuse is for the individual to ingest over-the-counter ephedrine tablets. On rare occasions, the pills might be crushed and the resulting power snorted. On even more rare occasions, the pills are crushed, mixed with water, and then injected into a vein.

Complications of Ephedrine Misuse

The therapeutic window for ephedrine is quite small, and, as indicated above, it can induce toxic effects even at therapeutic doses. Ephedrine misuse can result in impaired judgement, agitation, **necrosis**²⁰ of the lining of the gastrointestinal tract, nausea, vomiting, stroke, irritation of cardiac tissues (especially in individuals who have damaged their hearts due to misuse), potentially fatal heart arrhythmias, and heart attacks. The causal mechanism for ephedrine-induced heart attacks appears to be a drug-induced increase in cardiac muscle contractions, increasing the oxygen demand by those tissues. This is potentially dangerous if the person should have some form of coronary artery disease that independently limits the blood flow to the heart muscle.

Ephedrine misuse can also result in the formation of ephedrine-based kidney stones, which is seen in persons who use exceptionally large doses of ephedrine on a chronic basis. These kidney stones are found to be almost entirely ephedrine when they are examined by physicians, and are quite painful when they move down the urinary tract to the bladder.

THE AMPHETAMINE COMPOUNDS

Effects of Amphetamine Misuse

The amphetamine compounds, especially methamphetamine, might be ingested orally, used intranasally (i.e., "snorted"),

smoked, or injected intravenously. Depending on the individual's tolerance to the effects of the amphetamines, the individual might experience a state of heightened alertness, confidence, and euphoria. When smoked or injected, those who use methamphetamine report a sensation of a "whole body orgasm" (Gorelick, 2009). The effects of the amphetamines depend on factors such as (a) dose, (b) method of administration, (c) possible concurrent use of other compounds, (d) the individual's state of health, and (e) the individual's past substance use history.

Orally administered amphetamine compounds will begin to take effect in 20 minutes, while a snorted (intranasal) dose will begin to take effect in about 5 minutes. When injected or smoked, an amphetamine compound will take effect in a matter of seconds (Gorelick, 2009; Rawson & Ling, 2008). The amphetamines and related compounds are popular drugs to misuse on the college campus, especially as students prepare for examinations (Azar, 2008). Surprisingly, there is no evidence to suggest that these compounds actually improve the individual's performance on examinations. Students still misuse them around exam time in the hope that they will give them an "edge" as they study. Then, having discovered that these compounds allow them to remain awake for longer periods of time than is normal, the students use the amphetamines so that they might party longer (Azar, 2008).

During the 1970s much of the methamphetamine misused in the United States came from small "laboratories" that would produce relatively small amounts of methamphetamine using various easily obtained chemicals for local consumption.²¹ These "kitchen labs" proliferated in the 1990s when methamphetamine again became a popular drug. However, the process of making methamphetamine is dangerous, and even legitimate pharmaceutical companies will suffer the occasional explosion in a production facility. Illicit laboratories are much more likely to experience an explosion during the manufacture process. So common are the explosions of labs that local police departments often wait for the explosion to help them identify a methamphetamine production site.

Unfortunately, methods and the necessary materials for methamphetamine production are available on the internet. "Nazi meth" is one such preparation of illicit methamphetamine. The name is obtained from the Nazi symbols that decorated the paper on which the formula was originally written ("Nazi meth on the rise," 2003).

¹⁹This assumes that the individual is taking *only* ephedrine.

²⁰See Glossary.

²¹It has been estimated that for every pound of methamphetamine produced, 5–7 pounds of toxic waste are also produced, which then becomes an expensive hazardous waste problem for the community where the "lab" was located (Rollo, Sane, & Ewin, 2007).

Unlike some of the other formulas for methamphetamine manufacture, this method does not rely on the use of red phosphorus,²² but rather uses lithium (obtained from batteries) and ammonia (“Nazi meth on the rise,” 2003). The use of these compounds for the production of illicit methamphetamine exposes the individual using the compound to various contaminants²³ (Graber, 2007). To combat the production of illicit methamphetamine, precursor compounds such as ephedrine and pseudoephedrine were placed under strict control in the United States. Individuals are now only able to purchase a small amount of pseudoephedrine each month for self-medication of colds or allergies. The impact of this restriction has been minimal at best (Cunningham et al., 2009), and illicit methamphetamine remains rampant.

There is a financial incentive for producing illicit methamphetamine. An investment of \$200 in the chemicals used for such illicit production might produce enough to sell for \$2,500 on the illegal market. This financial incentive attracted the attention of organized crime cartels, which set up large-scale production facilities (known as “super labs”) in Mexico, and then the methamphetamine is smuggled across the border (Graber, 2007). These super labs have essentially replaced the smaller production facilities once commonly found in the United States, although on occasion they are still discovered by police.

Methods of Amphetamine Misuse

There are multiple methods of amphetamine misuse. The amphetamine molecule is easily absorbed through the gastrointestinal tract, and thus oral administration is one common method by which the amphetamines are misused. The amphetamines are also well absorbed from intramuscular injections, the nasal mucosa, through the lungs if it is smoked, and from the general circulation if it is injected into a vein. When smoked, the amphetamine molecule is able to cross into the circulation easily, where it is then transported to the brain in a matter of seconds. When injected into a vein, the amphetamine molecule is also able to reach the brain in just a few seconds. Amphetamine smoking and intravenous injection are the most common methods of amphetamine misuse in the United States (Rollo et al., 2007). The amphetamine molecules are also easily absorbed through the tissues of the nasopharynx, allowing them to be snorted (Rollo et al., 2007). Although it might be absorbed through the tissues of the rectum, this is not a popular method of amphetamine administration.

²²Usually obtained from matches.

²³The exact contaminants in illicit methamphetamine varies from one batch to another.

Subjective Effects of Amphetamines When Misused

The subjective effects of amphetamine misuse depend on several factors, including (a) possible concurrent substance use, (b) whether the individual has developed any degree of tolerance to the amphetamines, (c) the method by which s/he uses the compound, (d) the purity of the compound being used, (e) the method of administration, (f) the dose administered, (g) the duration of amphetamine use, (h) the individual's expectations for the substance, and (i) the individual's state of health. All of these factors interact with the individual's expectations for the drug to produce the subjective drug experience. Individuals who use intravenous amphetamine frequently report a period of intense, almost orgasmic feeling at first, followed by a gentle state of euphoria following the drug's administration. Persons who take amphetamines orally or who snort it have reported just the sense of gentle euphoria, which may last for a number of hours. In the case of methamphetamine, this “high” might last for 8–24 hours, a feature of this compound that makes it more addictive than cocaine²⁴ (Castro, Barrington, Walton, & Rawson, 2000; Rawson, Dodano, & Hillhouse, 2005). Individuals misusing these compounds also report feeling less need for sleep and a reduced appetite. These are the effects that make amphetamine misuse desirable to the individual.

Individuals who misuse amphetamine quickly become tolerant to the euphoric effects of these compounds (Haney, 2004). In an attempt to recapture the initial sense of euphoria, many individuals misusing these compounds engage in binge amphetamine use (Gorelick, 2009). Others who misuse amphetamines “graduate” from the oral use of these compounds to intranasal use, smoking, or even injection. When those who inject amphetamines become tolerant to the effects of the amphetamine being misused, they might embark on a “**speed run**,” injecting more amphetamine every few minutes. In many cases, the cumulative dose injected within a 24-hour span of time might be enough to kill a drug-naïve person, and are well within the range of neurotoxicity found in animal studies (Haney, 2008). Such speed runs might last for a number of hours, or even days, after which time the individual will usually fall into a state of deep sleep and/or depression that might reach suicidal proportions.

CONSEQUENCES OF AMPHETAMINE MISUSE

Because the amphetamines have a reputation for enhancing normal body functions (increased alertness, concentration, etc.), they are mistakenly viewed by some individuals as being less dangerous than other illicit compounds (United Nations, 2011). Unfortunately, there is a significant interindividual

²⁴Discussed in the next chapter.

variability for the development of amphetamine toxicity, with some individuals demonstrating evidence of toxic reactions at therapeutic dosage levels (Breggin, 2008). We will look at the toxic effects of amphetamine misuse on the major body organs in the sections below.

Brain Damage

Researchers have found that the misuse of any amphetamine can cause damage to the brain on both a regional and a cellular level, although it is not clear whether some of the amphetamine compounds are more likely to cause this effect than others (Yudko, Hall, & McPherson, 2009). Fatovich and colleagues (2010) found that at least one in five individuals who misused methamphetamine had a lesion in the brain when examined by magnetic resonance imaging (MRI), although the significance of these findings was not clear, as the authors admitted.

At the neural level, even at low dosage levels, the amphetamines have been found to damage or destroy up to 50% of the dopamine-producing neurons (Rawson et al., 2005). The danger of neurotoxicity from methamphetamine appears to be dose-related and is greater at higher doses of the compound (Hanson & Fleckenstein, 2009). At high doses, the amphetamine compounds, especially methamphetamine, also appear to be highly toxic to both the serotonergic neural networks (Yudko et al., 2009). Animal research has found that dopamine and norepinephrine neurotransmitter levels might not return to normal for at least 6 months of abstinence from further amphetamine use (King & Ellinwood, 2005), yet determining whether there is a similar impact in humans needs further research (Kish, Boileau, Callaghan, & Tong, 2017). It has been found that individuals who abused an amphetamine compound at some point in their lives had a three-fold higher risk for the development of Parkinson's disease later in life (Curtin et al., 2015; Wilson, Shannon, & Shields, 2017).

The causal mechanism for this neurotoxicity is not clear, and there are at least two competing theories to account for this observed effect. One theory suggests that at high dosage levels methamphetamine and similar compounds will induce the release of peroxide and hydroxyquinone family of compounds, both of which function as "free radicals" at the synaptic junction (Ling et al., 2006). In theory, these toxins might then poison the neurons (especially those in the serotonergic neurotransmission system), inducing neural death (Jaffe, Ling, & Rawson, 2005; King & Ellinwood, 2005). A competing theory is that high doses of an amphetamine compound force the release of large amounts of glutamate, which in large amounts is known to be neurotoxic. A newer theory includes the consideration of the impact not only on the nervous system, but also within the immune system and gut (Prakash et al., 2017).

Methamphetamine addicts have been found to have a significant reduction in the "**gray matter**" in the brains²⁵ on high-resolution magnetic resonance imaging (MRI) tests when compared with age-matched control subjects (Thompson et al., 2004). The amphetamines have been implicated as the cause of temporary and permanent changes in cerebral blood flow patterns (Buffenstein, Heaster, & Ko, 1999; Payer & London, 2009), as well as cerebral vasculitis and cerebral vasospasm. There is also a known relationship between amphetamine abuse and strokes (Lezak, Howieson, Bingler, & Tranel, 2012), with individuals who misuse amphetamines being at 200% higher risk for a stroke than individual who do not misuse amphetamines. High doses of methamphetamine might break down the blood-brain barrier,²⁶ increasing the risk of neurotoxicity and possible cerebral infections. Further, there is evidence of specific alterations in brain function, with some regions of the brain increasing in size during periods of active amphetamine misuse. This is thought to reflect localized trauma to regions of the brain such as the parietal cortex and caudate nucleus induced by long-term amphetamine misuse (Jernigan et al., 2005).

The team of Hart, Marvin, and Smith (2012), found **statistically significant**²⁷ impairment on only a small number of cognitive functions in those who misused amphetamines as compared with a control sample. The authors noted that the observed differences still fell within the normal range based on normative data for the measure(s) being used. Finally, the authors raised the possibility that researchers have a preconceived belief that *any* observed differences between those who misuse methamphetamine and control participants on the measure(s) being used in their study *must* be due to the methamphetamine misuse, a preconception that might have clouded the researchers judgment of the implications of their findings. Thus, the issue of whether methamphetamine misuse causes cognitive decline has yet to be definitively settled. It has been demonstrated that methamphetamine can induce agitation, delirium, and seizures²⁸ (Engel, 2013; Graber, 2007; Virani, Bezchlibnyk-Butler, & Jeffries, 2009). Following methamphetamine cessation, many individuals report having trouble concentrating. It has been assumed that any degree of improvement in cognitive

²⁵See Glossary.

²⁶See Glossary.

²⁷Statistically significant differences are not always clinically significant differences if both scores fall in the normal range. The difference between an IQ of 110 and an IQ of 115 is statistically significant, but in real life is that difference of any real importance?

²⁸If the user has a preexisting seizure disorder, the amphetamines are capable of lowering the seizure threshold and induce seizures even if the user is compliant with their antiepileptic medication regimen. See *epileptogenic* in Glossary.

function must be attributed to the fact that the individual has abstained from alcohol and drug misuse for at least a year (Salo, Nordahl, Galloway, Moore, et al., 2009).

Also, there are rare reports of amphetamine-induced episodes of the **serotonin syndrome**,²⁹ which is potentially life-threatening. Individuals who misuse amphetamines appear to be at increased risk for the development of Parkinson's disease (Lezak et al., 2012). Further, long-term amphetamine misuse can induce sleep disturbances that can persist for a number of months after the last use of such drugs.

Consequences of Amphetamine Misuse on the Emotions

Individuals who misuse amphetamines will often experience periods of deep depression between periods of active amphetamine use (Rawson et al., 2005). These depressive episodes can reach suicidal proportions. Further, the misuse of amphetamines can cause the individual to experience significant levels of anxiety, and possibly panic attacks (Ballas, Evans, & Dinges, 2004; Breggin, 1999). Amphetamine-induced anxiety episodes may persist for weeks or even years after the individual's last use of an amphetamine, possibly because of drug-induced sensitization of those regions of the brain involved in the anxiety response (London et al., 2004). Often, the individual misusing amphetamines will attempt to control drug-induced anxiety through anxiolytics, marijuana, or alcohol, complicating their medical care.

During periods of active amphetamine misuse, the individual might experience periods of drug-induced confusion, irritability, fear, suspicion or outright paranoia, hallucinations, or delusional thinking (Gorelick, 2009; Julien, 2005; King & Ellinwood, 2005; Miller, 2005). Other consequences of amphetamine misuse include agitation, assaultiveness, tremor, headache, irritability, weakness, suicidal and homicidal tendencies (Albertson, Derlet, & van Hoozen, 1999; Ballas et al., 2004; Rawson et al., 2005). The amphetamines as a group have the potential to induce a psychotic state which in its early stages is often indistinguishable from paranoid schizophrenia. The risk for the development of an amphetamine-induced psychosis appears to be strongest in those using methamphetamine, but it can also be induced by the misuse of other amphetamine compounds (Ballas et al., 2004; Bartki, 2001; Kosten & Sofuoglu, 2004). McKetin, Lubman, Baker, Dawe, and Ali (2013) concluded that individuals using methamphetamine were 5.3 times more likely to develop psychotic symptoms during periods of active methamphetamine misuse as compared with those who do not use methamphetamine. The authors also noted that there was a dose-related risk for the development of a methamphetamine

psychosis, with the highest risk being seen in those persons who misuse methamphetamine at higher doses.

Symptoms of an amphetamine-induced psychosis can result in symptoms as confusion, suspiciousness, paranoia, auditory and/or visual hallucinations, delusional thinking, anxiety, and possibly aggressive behavior (Haney, 2008; Iverson, Iverson, Bloom, & Roth, 2009; King & Ellinwood, 2005; United Nations, 2011). Less common symptoms of an amphetamine-related psychosis include psychomotor retardation, incoherent speech, inappropriate or flattened affect, and depression (Srisurapanont, Marsden, Sunga, Wada, & Monterio, 2003). Chronic misuse of any amphetamine compound can induce a condition known as **formication**³⁰ (Fadem, 2009; Tekin & Cummings, 2003). Individuals with this condition have the subjective sensation of having bugs crawling on or just under their skin, and have been known to scratch or burn their skin in an attempt to rid themselves of these unseen creatures. The experience of formication appears to reflect the drug-induced over-stimulation of the nervous system.

The amphetamine psychosis usually clears within a few days to a few weeks after the cessation of drug use, although Rawson and Ling (2008) suggested that in 28% of cases this condition might last longer than 6 months and might become permanent (Haney, 2004; Rawson et al., 2005). There was an epidemic of amphetamine misuse in Japan following the end of World War II, and during this time researchers noted that the amphetamine psychosis required up to 5 years to clear in 15% of the cases (Flaum & Schultz, 1996). Using positron emission tomography (PET) scans, Sekine and colleagues (2001) were able to document long-lasting reductions in the number of dopamine transporter molecules in the brains of those who had used methamphetamine. The authors suggested that this might be one mechanism through which methamphetamine misuse is able to induce a psychotic state. It was once thought that intravenous diazepam and haloperidol were the most effective in treating the toxic reaction to an amphetamine (Brust, 2004). However, further evidence suggested that haloperidol might be neurotoxic to the cells of the substantia nigra region of the brain when used to treat amphetamine-induced psychotic states (Hatziperos, Raudensky, Soghomonian, & Yamamoto, 2007). More recently, aripiprazole and risperidone have been investigated for the treatment of amphetamine-induced psychosis (Wang, Zhang, et al., 2016), while metoprine is being investigated for use for methamphetamine overdoses (Kitanaka, Kitanaka, Hall, Uhl, & Takemura, 2016).

It was once thought that amphetamine-induced psychotic symptoms were rare. But researchers have found that

²⁹See Glossary.

³⁰See Glossary.

two-thirds of persons with a methamphetamine use disorder (MUD) will report at least some symptoms of a psychotic reaction upon detailed inquiry (Rawson et al., 2005). Again, it is not known whether other members of the amphetamine family of compounds share this characteristic or not. There is also evidence that methamphetamine-related aggression may appear both during periods of acute intoxication, especially during the toxic psychosis, and during the withdrawal stage (Sekine et al., 2001, 2006). There is an interesting body of research suggesting that high doses of methamphetamine are less likely to induce an aggressive response than are lower doses (Yudko et al., 2009). Amphetamine-related aggression is thought to reflect reductions in the serotonin transporter system in the brain, and that such changes in the serotonin transporter system seem to continue for at least a year after the individual's last amphetamine dose (Sekine et al., 2006). Further research is needed to determine the causes and clinical course of amphetamine-induced aggression.

The Digestive System

The amphetamines have a long history of being prescribed as anorexic agents to aid in weight-loss programs, but their misuse can also result in such problems as diarrhea, constipation, nausea, vomiting, and ischemic colitis (Rawson et al., 2005; Sadock et al., 2015). Further, because of their anorexic side effect, individuals who misuse these compounds tend to neglect their daily dietary requirements, developing various dietary deficiencies as the body's stores of protein, various vitamins, and amino acids are depleted (Mooney, Glasner-Edwards, Rawson, & Ling, 2009).

Methamphetamine misuse is associated with acute abdominal pain and gastroduodenal ulcers that sometimes can reach impressive size (Mooney et al., 2009). A poorly understood consequence of long-term methamphetamine misuse is a condition known as "meth mouth" (Davey, 2005; Graber, 2007; Rawson et al., 2005). Individuals who suffer from this condition rapidly develop so much tooth decay or damage that extensive dental repairs and extractions are often necessary. There are several competing theories about the cause of meth mouth. First, methamphetamine misuse reduces saliva production to about one-fourth its normal level.³¹ This interferes with saliva's role as a defense against dental decay. A second theory is that because those who use methamphetamine substitute sugar-sweetened soda and candy for food, this increases their risk for dental decay (Rawson et al., 2005). A third possibility is that the compounds used to manufacture illicit methamphetamine cause or exacerbate dental decay, sometimes to the point where it becomes necessary to remove the individual's teeth and insert dental prosthetics

(Davey, 2005; Rollo et al., 2007). This might reflect the fact that the first dental care the individual receives for many years is when s/he is first incarcerated.

The Cardiovascular System

There is strong evidence that individuals who misuse amphetamines are at higher risk for a myocardial infarction³² than those who do not misuse these compounds. The team of Westover, Nakonezny, and Haley (2008) examined the records of 3 million 18–44-year-old adults from the state of Texas, and concluded that those who misused amphetamines were 61% more likely to suffer a myocardial infarction than those of the same age who did not use amphetamines. One possible causal mechanism is the ability of compounds like methamphetamine to join sugar molecules to protein molecules (Treweek, Wee, Koob, Dickerson, & Janda, 2007). This then alters the function of those protein molecules, possibly causing them to become toxic to the muscle cells of the heart. This hypothesis would seem to be supported by the work of Turdi and colleagues (2009), who found that methamphetamine alters biochemical processes necessary for proper cardiac muscle contraction, including the role of many proteins. This may also be one mechanism through which the abuse of methamphetamine can induce cardiac arrhythmias. Another phenomenon seen in some individuals who use methamphetamine is sudden cardiac death. Faith, Jiin-Cherng, Chan, and Chang (2012) offered the hypothesis that this phenomenon is the result not of damage to the heart itself, although that is often found in those who use amphetamines, but to the failure of brain stem cardiovascular regulation.³³

Long-term amphetamine misuse, but especially the misuse of methamphetamine, has been implicated in the acceleration of plaque development in the coronary arteries of the user, contributing to coronary artery disease for the individual (Karch, 2009). Amphetamine misuse can also result in hypertensive episodes, tachycardia, arrhythmias, and sudden cardiac death when misused at high doses (Ballas et al., 2004; Brust, 2004; Fadem, 2009; Gitlow, 2007; Karch, 2009; Rawson et al., 2005). Other suspected cardiac complications from amphetamine misuse include cardiac ischemia, myocardial ischemia, angina, acute aortic dissection, and possible congestive heart failure (Acosta, Haller, & Schnoll, 2005; Diercks et al., 2008; Oehmichen, Auer, & Konig, 2005; Wadland & Ferencik, 2004). Individuals who misuse methamphetamine have frequently been found to suffer

³¹A condition known as xerostomia.

³²Commonly called a "heart attack."

³³The rostral ventrolateral medulla region of the brain stem is responsible for blood pressure regulation and control of the sympathetic nervous system. If this region of the brain stem is damaged, cardiac arrest cannot be reversed, and the rest of the body then dies from what appears to be cardiac arrest.

from “small vessel disease,” which is to say micro-infarcts that individually do not seem significant but which collectively reduce the heart’s effectiveness. This is why those who misuse methamphetamine have a 350% higher incidence of **cardiomyopathy**³⁴ than those of the same age who do not use methamphetamine (Yeo et al., 2007).

Amphetamine-induced hypertensive episodes are associated with an increased risk of stroke for the user. Amphetamine-related hypertension places stress on the walls of cerebral blood vessels, and if they are weakened by a birth defect, there is a danger of a hemorrhagic stroke as the weakened artery wall ruptures (Johnston & Elkins, 2008). Methamphetamine-related strokes are predominantly (but not exclusively) seen in the frontal lobes of the brain of the abuser (Mooney et al., 2009). Rare cases of methamphetamine-related cortical blindness have also been identified, as well as rare reports of subarachnoid hemorrhages (Mooney et al., 2009).

Effects of Amphetamine Misuse on the Pulmonary System

Amphetamine misuse has been identified as the cause of such respiratory problems as sinusitis, pulmonary infiltrates, pulmonary edema, exacerbation of asthma in patients with this condition, pulmonary hypertension, and possible pulmonary hemorrhage or infarct (Acosta et al., 2005; Rawson et al., 2005). Methamphetamine smoking has been identified as the cause of shortness of breath, some forms of pneumonia, and emphysema, possibly as a consequence of crushing tablets for smoking, thus admitting talc and other foreign agents into the lungs (Mooney et al., 2009).

Other Consequences of Amphetamine Misuse

Abuse of the amphetamines has been identified as a possible cause of rhabdomyolysis in some individuals, although the causal mechanism remains unclear at this time (Mooney et al., 2009). Amphetamine misuse has also been implicated as the cause of sexual performance problems for both men and women (Albertson et al., 1999; Finger, Lund, & Slagle, 1997; Sadock et al., 2015). In men, the chronic use of high doses of amphetamine compounds can cause an inhibition of orgasm for both sexes, and an inhibition of ejaculation in men. Individuals who misuse the amphetamines at high doses are at high risk for episodes of potentially fatal body hyperthermia (Ballas et al., 2004; King & Ellinwood, 2005; Rawson & Ling, 2008; Winslow, Voorhees, & Pehl, 2007).

There is evidence suggesting that methamphetamine misuse can cause liver damage (Karch, 2009; Pateria, de Boer, & MacQuillan, 2013; Rawson & Ling, 2008). Researchers have found that a “fatty liver” was present in 15.4% of individuals who used methamphetamine, and that 9% of those

who used methamphetamine demonstrated frank cirrhosis of the liver (Karch, 2009). However, most individuals who use methamphetamine use multiple drugs, and it is hard to determine whether methamphetamine itself is the cause of the observed liver damage, or just one of a range of compounds that induce the observed liver damage. Other identified consequences of amphetamine misuse include agitation and muscle twitching (Graber, 2007), and rarely hemorrhagic pancreatitis (Mooney et al., 2009).

The Addiction Potential of Amphetamines

There is no test by which a person might assess their potential to become addicted to these compounds, and if only for this reason, even the experimental use of amphetamines is not recommended. There is evidence, however, that the amphetamines might induce an addiction in less time than cocaine (Payer & London, 2009). When misused, these compounds stimulate the brain’s reward system (Haney, 2004), which is one of the reasons they are such popular drugs. This effect, plus the brain’s natural tendency to form strong memories of things that triggered the reward system, help sensitize the individual to drug use “cues.” Brust (2004) suggested that some individuals progress from their initial amphetamine misuse on through to full amphetamine addiction in just a few months, underscoring the addictive potential of these compounds.

Amphetamine Abstinence Syndrome

Following extended periods of amphetamine misuse at high doses, individuals will experience a withdrawal syndrome including **anhedonia**,³⁵ irritability, depression (which might reach suicidal proportions), fatigue, increased need for sleep, sleep disturbance, REM “rebound,” and poor concentration (Brust, 2004; Miller, 2005). Post-amphetamine misuse anhedonia might last for a period of months after the individual’s last amphetamine use (Miller, 2005; Schuckit, 2006a). Other symptoms noted in the first few days following extended periods of amphetamine abuse include musculoskeletal pain, anorexia, “craving” for amphetamines, and impaired social function. These symptoms wax and wane in intensity over the first few weeks of abstinence (Brust, 2004). The amphetamine abstinence syndrome is noted for all cases where the individual was misusing an amphetamine at high doses for extended periods of time, although it is strongest in those individuals who misuse methamphetamine.

“ICE”

“Ice” is a form of methamphetamine prepared for smoking. The chemical properties of methamphetamine allow for it to be concentrated in a crystal that resembles a chip of ice (thus the name) or a piece of clear rock candy. The chip of concentrated

³⁴See Glossary.

³⁵See Glossary.

methamphetamine is smoked, allowing the fumes to gain rapid access to the lungs and thus the general circulation, where it is transported to the brain in a matter of seconds. The practice of smoking ice apparently began in Japan following World War II, and knowledge of the practice was carried back to Hawaii by troops involved in the postwar occupation of Japan. The practice became popular in Hawaii, and eventually spread to the continental United States, where it became popular in some parts of the country (Karch, 2009).

In the United States, the wave of ice use went through three different phases: (1) In the earliest stages it was manufactured in Mexico and California, then shipped to various parts of the country (Rutkowski & Maxwell, 2009). (2) As the demand increased, local meth labs developed to meet local demand. The government has placed restrictions on precursor chemicals used in the production of methamphetamine such as pseudoephedrine, reducing local production to a limited degree. However, in spite of these restrictions, about 35% of illicit methamphetamine used in the United States is produced through small, clandestine operations using precursor chemicals such as pseudoephedrine and as few as two pieces of equipment. (3) The major sources of methamphetamine have moved to Mexico, and large amounts of the drug are then smuggled into the United States for consumption through a variety of routes.

How “Ice” Is Misused

Ice is a colorless, odorless, concentrated form of crystal methamphetamine. It is usually smoked, allowing the individual to titer effects to suit his/her perceived needs. Ice is usually less expensive than cocaine on a per-dose basis since it will last longer than cocaine when smoked (Rawson et al., 2005). Because of its duration of effect, it is *perceived* to be more potent than crack cocaine by the individual who has used both substances. It does not require the elaborate equipment necessary for cocaine smoking, and does not produce a smell to alert others that it is being used. Finally, if the individual should decide to stop smoking a “chip,” it will reform as a crystal as it cools, allowing for the remainder to be used at another time. As will be discussed in the next chapter, when smoked, cocaine will burn off almost immediately, forcing the individual to use it all at once. Thus, the preferred method of methamphetamine misuse is smoking, although it may also be injected. On occasion, the chip of methamphetamine is melted down into a liquid and injected intravenously. This is usually seen if other forms of methamphetamine are not available to the individual.

Subjective Effects of “Ice”

In contrast to cocaine-induced euphoria, which will last only 20 minutes, the euphoria induced by methamphetamine smoking is reported to last for hours. This is consistent with the pharmacological differences between cocaine and the

amphetamines, in that the stimulant effect of cocaine lasts for a short period of time, while that of an amphetamine compound might last for a period of hours.

The complications of methamphetamine smoking are essentially extensions of those seen with other forms of amphetamine misuse, since ice is simply a form of methamphetamine, and as such it shares the same side-effect and overdose profiles as other forms of amphetamine. Some individuals have reported experiencing a myocardial infarction up to 36 hours after their last use of ice, although the causal mechanism is not clear (Tominaga, Garcia, Dzierba, & Wong, 2004). Thus, ice shares the potential for incredible physical, social, and emotional damage seen with the misuse of other forms of the amphetamines.

METHYLPHENIDATE

Methods of Methylphenidate Misuse

The most common method of methylphenidate misuse is for the individual to take nonprescribed tablets orally or for the patient to take more than has been prescribed. On occasion, the tablets are crushed and then injected (Bjarnadottir et al., 2015), either alone or in combination with other drugs being injected.

Effects of Methylphenidate When Misused

Methylphenidate is a favorite stimulant for students who wish to “cram” before an examination, although on occasion it is misused for other reasons (Vedantam, 2006). Individuals who are using the substance for the high will often crush the pills into a fine powder, then either inhale the powder or inject it into a vein (Bjarnadottir et al., 2015; Karch, 2009; Stahl, 2008; Volkow & Swanson, 2003). The strongest effects are achieved when the compound is injected into a vein. When injected, methylphenidate can induce a 50% blockade of the dopamine transport system within seconds, inducing a feeling of euphoria for the user (Volkow & Swanson, 2003; Volkow et al., 1998). For many individuals, this drug-induced sense of euphoria becomes desirable, serving as a source of motivation for further methylphenidate misuse.

Consequences of Methylphenidate Misuse

One unanticipated consequence of methylphenidate misuse is physical addiction to this compound. Kim and colleagues (2009) administered methylphenidate to mice and found at the end of their trial period that the mice that received the methylphenidate had developed a greater number of spiny neurons in the nucleus accumbens than had the control mice. This is a region of the brain known to be associated with addiction to chemicals. However, the impact of this compound on the brain varies with the individual’s motivation to use it: Patients who receive this medication for the control of ADHD usually do not develop signs of addiction

to methylphenidate, while individuals who misuse it for recreational purposes are prone to do so. This might reflect the timing or dosage of methylphenidate used by these individuals as opposed to patients on this compound, or it might reflect another, as yet unidentified, process.

The physical consequences of methylphenidate misuse are essentially an extension of those seen when this compound is used medically. Even when used under a doctor's supervision, at recommended dosage levels, methylphenidate can occasionally trigger a toxic psychosis, with symptoms similar to those seen in paranoid schizophrenia (Aldhous, 2006; Karch, 2009). Most certainly, large doses, such as those seen when this compound is misused, can trigger a toxic psychosis as well (Weiss, 2007). A small percentage of individuals will experience a methylphenidate-induced stroke or cardiac problems (Karch, 2009). When individuals who misuse methylphenidate crush a tablet to use intravenously, they will inject not only the active agent of the compound, but also various "**fillers**"³⁶ designed to give the tablet shape and form (Volkow et al., 1998). The fillers may then form a thrombosis, causing damage to body tissues that depend on the now blocked artery for oxygenated blood and food. Sometimes such damage occurs in the retina, causing visual field disturbance and possibly blindness (Karch, 2009). As this information would suggest, methylphenidate is not a safe compound, and the individual takes on a very real risk of potential harm and addiction when s/he misuses this compound.

CNS Stimulant Misuse and the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) (American Psychiatric Association, 2013) classified the CNS stimulants as including amphetamines or amphetamine-like compounds, as well as cocaine. The DSM-5 identified five patterns of CNS stimulant abuse:

- Stimulant (CNS) use disorder
- Stimulant intoxication
- Stimulant withdrawal
- Other stimulant-induced disorders
- Unspecified stimulant-related disorder

Of these five categories of CNS stimulant misuse, the *stimulant use disorder* refers to what was earlier identified as either

stimulant abuse or dependence on a CNS stimulant, some of the symptoms of which include the development of tolerance over time, recurrent use of the stimulant in situations where its use is known to be hazardous, a characteristic withdrawal syndrome, and continued use in spite of awareness of the drug's negative effects on the individual's vocational, academic, social, occupational or familial duties, to name a few of the criteria that must be met. Of the 11 criteria suggested by the American Psychiatric Association (2013), the individual would need to meet two within a 12-month period for a diagnosis of a stimulant use disorder. Modifiers to the diagnosis include whether the individual is in early or sustained remission, and if the individual was in a controlled environment where access to these compounds was difficult.

The DSM-5 then identifies whether the individual's addiction to the stimulant was mild, moderate, or severe, further breaking down the list for the misuse of an amphetamine compound, cocaine, or an unspecified compound with appropriate ICD-10 classification numbers for each condition. In rare cases, physical dependence on a CNS stimulant has developed after just one week of continuous use (American Psychiatric Association, 2013), and so the length of time that a person has misused a stimulant should not be used as a yardstick to assess whether they are potentially addicted to one of these compounds or not. The development of tolerance and a withdrawal syndrome are more reliable markers of a *stimulant use disorder*, in the opinion of the author of your text.

The DSM-5 does warn that the stimulant use disorders often mimic the manifestations of primary psychiatric disorders such as major depression or schizophrenia, making the differential diagnosis of a stimulant use disorder difficult. As noted above, initially individuals experiencing *stimulant intoxication* will report feelings of increased energy and well-being. The signs of stimulant intoxication are discussed in this chapter as well as in the DSM-5. The physical manifestations of CNS stimulant misuse and potential dangers associated with the misuse of these compounds are as identified in this chapter or in Chapter 9 for cocaine.

Stimulant withdrawal develops within a few hours of the individual's last use of a CNS stimulant, and the symptoms reviewed in this chapter should be interpreted as a sign of stimulant withdrawal only if the individual does not suffer from a medical condition that might induce such symptoms, according to the DSM-5. *Other stimulant-induced disorders* are conditions that resemble symptoms of other psychiatric conditions that are caused by the misuse of stimulants. An excellent example would be the depressive symptoms that develop during stimulant withdrawal that normally resolve after the withdrawal process has ended. Finally, the *unspecified stimulant-related disorders* reflect cases where the individual's stimulant use causes impairment in social, occupational,

³⁶See Glossary.

familial, or vocational life, but which do not meet the criteria for a *substance use disorder* diagnosis.


Chapter Summary

There are a number of compounds that function as central nervous system stimulants, including the natural substance ephedrine, which was isolated from the ephedra plant. This was found to be useful in the treatment of asthma, but fears developed that the demand for ephedrine might outstrip supply. Chemists examined compounds that had similar chemical structures in the hopes of finding substitutes. The analogs of ephedrine known as the amphetamines were isolated in the 1880s, but it was not until the early 1930s that they were introduced for the treatment of asthma. Later, these compounds were also found to have a paradoxical calming effect on some children who were behaviorally challenging.

Individuals who misused drugs also found that the effects of the amphetamines were similar to those of cocaine, which was already known to be quite dangerous. The

ampules of amphetamine-containing liquid could be carefully unwrapped, broken open, and the contents might be injected, providing a “high” similar to that seen with cocaine, but that lasted for a longer period of time. At the same time, physicians were prescribing amphetamines for their anorexic side effect, and as an aid to the treatment of depression. As physicians have come to better understand the misuse potential of amphetamines, they have come under increasingly strict controls.

Unfortunately, the amphetamines can also be easily manufactured in illicit laboratories, so when individuals addicted to these substances were unable to gain access to pharmaceutical quality amphetamines, they switched to illicit sources of these compounds, and there continues to be a thriving manufacture/distribution system for the amphetamines. The most commonly misused amphetamine is methamphetamine, although the other members of the amphetamine family are also misused. The current generation of individuals misusing these substances have come to relearn the lesson that individuals who misused them in the 1960s had discovered through grim experience: “Speed kills.”



CHAPTER 9

Cocaine Misuse and Cocaine Use Disorder

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 9.1 Understand the history of cocaine
- 9.2 Describe the scope of the problem of cocaine use and misuse
- 9.3 Comprehend the pharmacology and methods of use of cocaine
- 9.4 Describe the subjective effects of cocaine use
- 9.5 Understand the complications of cocaine misuse

Introduction

Future historians will note that there have been at least three distinct cocaine use “epidemics” in the United States. Each comprised several phases: (a) the warnings of earlier generations of those who used cocaine were ignored, (b) cocaine became a rare drug to misuse, (c) its misuse became more widespread, (d) the warnings of earlier generations were confirmed, (e) cocaine misuse was again deemed to be both dangerous and not a panacea, and (f) its misuse became less and less common until it was again a rarely misused compound.

This cycle is clearly seen in the United States in the last century. Cocaine misuse was common in the first decade(s) of the 20th century, and its dangers were well known to those who used illicit drugs as well as physicians. In the 1930s, the recently introduced amphetamine compounds became the stimulant of choice, in part because they were reputed to be a safe alternative to cocaine. As the dangers associated with amphetamine misuse became known, there was a resurgence of cocaine misuse in the early to mid-1980s. This wave of cocaine misuse peaked around the year 1986, and then gradually declined as those using illicit drugs again returned to the misuse of the amphetamine compounds. Despite the downward trend in usage shown, for example, in twelfth graders in the United States, with only 3.7% indicating trying cocaine at some point at least once, the lowest percentage in more than 25 years (Johnston, O’Malley, Miech, Bachman, & Schulenberg, 2017), the cycle is likely to repeat itself in the future. The problem of cocaine misuse has never entirely disappeared. In this chapter, we will discuss the use and misuse of cocaine.

A Brief History of Cocaine

Biologists believe that at some point in the distant past a member of the plant species *Erythroxylon coca* began to produce a toxin in its leaves to protect itself from predation by insects or animals (Breiter, 1999). This neurotoxin, cocaine, is quite effective in this role, allowing the plant to thrive in the relatively thin atmosphere of the high Andes Mountains. Then, at least 5,000 years ago, it was discovered by early settlers of the region that by chewing the leaves of the coca plant, it was possible to ease feelings of fatigue, thirst, and hunger, allowing them to work for longer periods of time in the thin mountain air (Levis & Garmel, 2005).

When the first European explorers arrived, they discovered the thriving Incan Empire in what they called the New World. The coca plant was used extensively by these people, who believed it to be a gift from the sun god (Brust, 2004). The use of cocaine was generally reserved for the upper classes of Inca society when the first European explorers arrived and eventually conquered the Inca Empire (Brust, 2004). The conquerors soon discovered that by giving native workers coca leaves to chew on, they would become more productive, and they encouraged its widespread use for that reason. Even today, the practice of chewing coca leaves, or drinking a form of tea brewed from coca leaves, is commonplace in South America. Natives will chew coca leaves mixed with lime obtained from sea shells, a practice that helps to negate the bitter taste of the coca leaf itself. The cocaine that is released by the practice of chewing is then absorbed into the individual's system, providing a stimulatory effect that negates the fatigue normally felt when working at the high altitudes of the Andes. This practice may also allow the individual chewing the leaves to gain some small measure of nutritional benefit, although this has not been scientifically studied. European scientists took a passing interest in the coca plant, attempted to isolate the compound(s) that made it so effective in warding off hunger and fatigue, and in 1855¹ a chemist by the name of Albert Neiman isolated a compound that was later named cocaine. This accomplishment allowed scientists of the era to obtain large amounts of relatively pure cocaine for research purposes. One experiment was the injection of concentrated cocaine into the bloodstream using another recent invention: the hypodermic needle. The world has not been the same since.

By the late 1800s, extracts from the coca leaf were used to make a wide range of drinks and elixirs, one of which even won an endorsement from the pope himself (Martensen, 1996).

No less a figure than Sigmund Freud experimented with cocaine as a possible treatment for depression as well as a possible treatment for narcotic withdrawal symptoms. Freud later tried to warn others of his mistaken perception that cocaine was an effective treatment for these disorders, and that it was addictive, but was ignored by scientists of the era (Bjelić, 2017; Gold & Jacobs, 2005; Markel, 2011). Cocaine had entered European society, and even today it remains stubbornly entrenched as a drug to misuse.

The natives of the high Andes continue to chew cocaine leaves to help them work in the rarefied mountain air. Some researchers think the fact that they are able to discontinue cocaine use when they descend to lower altitudes is evidence that it is not very addictive. However, this argument is undermined by the fact that chewing the coca leaf is not an effective method of administration. Much of the cocaine that is released during coca chewing is destroyed by digestive juices and the first-pass metabolism process.² Still, the blood levels of cocaine obtained when cocaine leaves are chewed are at the lower end of the blood levels achieved when a cocaine abuser snorts cocaine powder, and while the amount of cocaine that reaches the brain is barely enough to have a psychoactive effect, cocaine chewers are still thought by some scientists to become addicted to it (Karch, 2009). Thus, the question of whether coca chewing results in cocaine addiction has not been resolved.

Cocaine in U.S. History

The history of cocaine use in the United States is, surprisingly, intertwined with attempts to control alcohol use by the town fathers of Atlanta, Georgia. In response to a prohibition against alcohol use on Sundays, John Stith-Pemberton developed a "temperance drink" (Martensen, 1996, p. 1615) which was alcohol-free but originally contained 60 mg of cocaine per 8-ounce serving (Gold, 1997). In time, the world would come to know Stith-Pemberton's product by the name of "Coca-Cola," and it has since become one of the more popular soft drinks sold.

The fact that Coca-Cola once contained cocaine is surprising to many modern readers. But it is important to keep in mind that at the turn of the 20th century, consumer protection laws were virtually nonexistent, and compounds such as cocaine and morphine were available without a prescription and were often hidden ingredients in a range of "patent" medicines and other products. This practice contributed to a wave of cocaine use in Europe between the years 1886 and 1891, and in the United States between 1894 and 1899, and again between 1921 and 1929. These

¹Schuckit (2006a) reported that cocaine was first isolated in 1857, not 1855.

²Discussed in Chapter 3.

waves of cocaine use and the resulting cocaine use disorders were fueled by the common practice of using cocaine as a hidden ingredient in so many products. Fears fueled by rumors that cocaine was corrupting Southern blacks prompted both the passage of the Pure Food and Drug Act of 1906 and the classification of cocaine as a “narcotic” in 1914 (Martensen, 1996). The Pure Food and Drug Act did not prohibit the use of cocaine in products, but it did require that the ingredients be identified on the label, allowing consumers to avoid products that contained compounds such as cocaine. This prompted many manufacturers to remove it from their products entirely. When the Harrison Narcotics Act of 1914 was passed, the nonmedical use of cocaine became illegal in the United States.

These regulations, combined with the geographic isolation of the United States in World War I prior to the entry of this country into that conflict, and the introduction of the amphetamines in the 1930s, virtually eliminated cocaine misuse in the United States. It did not resurface as a major drug of misuse until the late 1960s, when it was viewed as the “Champagne of drugs” (White, 1989, p. 34). As a new generation of individuals using illicit drugs discovered its euphoric effects in the 1970s and 1980s, it became increasingly popular as an illicit drug. Reports of the physical damage induced by cocaine misuse at the turn of the 20th century, or of its addiction potential, were dismissed as exaggerations, or, given the primitive state of medicine in the era, as being a misdiagnosis of another condition (Peele, 2010; Walton, 2002).

A concurrent and possibly contributing factor to the rise of cocaine was the growing disillusionment with the amphetamines that started in the mid-1960s. As drugs of misuse, the amphetamines had gained the reputation of being both dangerous and potentially fatal recreational substances. Individuals using illicit drugs would warn each other that “speed kills,” a reference to the dangers associated with the use of “speed” (the slang term for the amphetamines). Cocaine had gained a reputation as being able to induce the same sense of euphoria as the amphetamines without their dangers. This, plus the emerging restrictions on amphetamine production and use, and its reputation as a “glamour” drug, all helped focus the attention of those using illicit drugs on cocaine in the late 1960s.

By the middle of the 1980s, the cocaine distribution and sales network in the United States had become the seventh largest industry of its time, generating an estimated \$21 billion a year in profits. This in turn attracted the attention of what has come to loosely be called “organized crime.” Cocaine distributors were looking for ways to increase sales and to open new markets for their “product” in the United States. The primary method of cocaine use during this era was intranasal inhalation of cocaine powder, although some abusers

did smoke it after going through a long, dangerous process of transforming the powder into a smokable form of cocaine. After a period of experimentation, “crack” cocaine was developed. Essentially, **crack** is cocaine prepared for smoking before sale, and its misuse in the past accounted for as much as 50% of the illicit cocaine market in the United States (Greydanus & Patel, 2005).

The wave of cocaine misuse that swept across the United States in the 1980s and early 1990s is a topic worthy of a book in its own right, and will be mentioned only in passing in this text. Just as the recently introduced amphetamines were adopted as a replacement for the known dangers of cocaine in the 1930s, cocaine was viewed by some as a safe alternative to amphetamine misuse in the 1970s and 1980s. The wave of cocaine misuse peaked in the mid-1980s, and the numbers of individuals misusing cocaine in this country have slowly declined in the years since, after a minor peak in use the late 1990s (Johnston et al., 2017). A recent introduction of **synthacaines**, synthetic designer drugs developed in labs to have effects similar to cocaine (Deslandes et al., 2017), may also have an impact on future cocaine trends.

Current Medical Uses of Cocaine

Cocaine was once a respected pharmaceutical compound, used in the treatment of a variety of conditions. It was found to function as a local anesthetic by blocking the movement of sodium ions into the neuron, thus reducing or eliminating the ability of the neuron to transmit pain messages to the brain (Drummer & Odell, 2001). In this capacity, it was used by physicians in surgical procedures in the ear, nose, throat, rectum, and vagina. As a topical anesthetic, its effects would begin in about 1 minute, and would last for up to 2 hours (Wilson, Shannon, & Shields, 2011). Sigmund Freud exploited this characteristic of cocaine toward the end of his life when he struggled with cancer of the tongue (Stahl, 2008). Cocaine is still occasionally used by otolaryngologists,³ especially because of its vasoconstrictive and analgesic effects, but for the most part it has been supplemented by newer, safer, compounds.

Scope of the Problem of the Cocaine Use Disorders

The amount of land dedicated to the cultivation of cocaine around the world decreased in 2014, although the manufacturing of cocaine appears to continue to gradually rise (U.N.

³Ear, nose, and throat specialists.

Office on Drugs and Crime, 2017). Globally, an estimated 0.3 to 0.4% of the world's population are thought to have used cocaine in the past year (U.N. Office on Drugs and Crime, 2017). The vast majority of the world's production of cocaine was intended for the illicit drug market. Authorities have been able to interdict a significant proportion of the total amount of cocaine produced, forcing distributors to resort to ever more ingenious methods to transport their product, such as semi-submersible and submersible ships, and more recently, unmanned aerial vehicles, also known as drones (Shields, 2017).

North America has for some time been the largest consumer of cocaine in the world, although collectively Europe consumes approximately the same amount of cocaine as does the United States (U.N. Office on Drugs and Crime, 2017). However, those who acknowledge use of cocaine in the past year have recently decreased by approximately one-third (U.N. Office on Drugs and Crime, 2017). Based on prevalence surveys in the United States, adults between 18 and 25 are three times more likely to use cocaine as compared to all other age groups (Kosten & Sofuoglu, 2015), and men are three times more likely than women to use cocaine (U.N. Office on Drugs and Crime, 2017).

In spite of mass media campaigns to the contrary, cocaine is not automatically physically addictive. Perhaps 15% of those who begin to use cocaine will ultimately become addicted to it (Budney, Roffman, Stephens, & Walker, 2007), while 28% become regular users⁴ (Leamon, Wright, & Myrick, 2008). There are wide variations in the popularity of cocaine misuse around the United States. Despite a current decrease in use of cocaine in the country, cocaine remains a significant part of the illicit drug problem in the United States at this time.

Pharmacology of Cocaine

Cocaine is best absorbed into the body when administered as the water-soluble compound cocaine hydrochloride. After entering the circulation, it is quickly transported to the brain and other blood-rich organs of the body. The level of cocaine in the brain is usually higher than the blood plasma levels, especially in the first two hours following administration ("Cocaine and the brain," 1994; Karch, 2009). Cocaine's effects on the individual appear to be stronger when levels are rising, with the same blood concentration that

causes euphoria when the blood levels are rising causing **dysphoria**⁵ when the blood levels are falling (Karch, 2009; O'Brien, 2006).

The pharmacological effects of cocaine are quite short-lived. The effects of snorted cocaine begin in 3–5 minutes, peak in about 10–20 minutes, and last about an hour (Mendelson & Mello, 2010). Cocaine smoking and injected cocaine result in an almost instantaneous "rush" experience as the drug begins to work, and the half-life of injected or snorted cocaine is estimated to be between 30 and 90 minutes (Jaffe, Rawson, & Ling, 2005; Leamon et al., 2008). Mendelson and Mello (2008, 2010) offered a more conservative estimate of cocaine's half-life as between 40 and 60 minutes. The difference between these two estimates might reflect the significant interindividual variability in the speed with which the bodies of different individuals are able to biotransform and eliminate cocaine. During the process of cocaine biotransformation, the liver will produce about a dozen metabolites of cocaine (Karch, 2009). About 80% of a single dose of intravenously administered cocaine is biotransformed into either *benzoylecgonine* (BEG) or *ecgonine methyl ester* (Levis & Garmel, 2005). Between 5 and 10% of a single dose is eliminated from the body unchanged, and about 10% is biotransformed into other compounds that are of minor importance and will not be mentioned again. Neither of the primary metabolites of cocaine has any known psychoactive effect. BEG has a half-life of about 7.5 hours and might be detected in urine samples for 48–72 hours. Thus, urine toxicology tests usually attempt to isolate this cocaine metabolite rather than cocaine itself as evidence of cocaine use.

At the neural level, cocaine forces the release of dopamine stores from the **presynaptic**⁶ neurons involved in the reward network of the brain, establishing strong drug-centered memories (Brust, 2004). This makes clinical sense: In the natural world, it would be advantageous for sources of positive reinforcers such as food, water, or sex to produce a strong memory trace in the individual's brain so that s/he could find that positive reinforcer again when s/he wanted to. Unfortunately, cocaine misuse short-circuits this reward system, causing a reward cascade stronger than that produced by natural reinforcers (Haney, 2004). Animal-based research suggests that cocaine suppresses the action of gene 9A, which in effect locks the "pleasure center" of the brain into the "on" position (Maze et al., 2010). It is not known whether this same process is found in humans, but these findings are suggestive of one mechanism through

⁴Regular cocaine use is a stepping stone to a cocaine use disorder. Some individuals who use cocaine on a regular basis will become addicted, and others will step back from the brink of addiction. Thus, about half of those who use regularly will become addicted to it.

⁵See Glossary.

⁶See Glossary.

which cocaine is able to induce a craving for additional cocaine use.⁷

Cocaine's reinforcing effects appear to involve those neurons that use dopamine as their primary neurotransmitter. There are at least five subtypes of dopamine receptors in the brain, and cocaine's reinforcing effects appear to involve the dopamine D1 receptor subtype (Romach et al., 1999). The authors administered an experimental dopamine D1 blocking compound to volunteers who acknowledged misusing cocaine, and discovered that they failed to experience any major euphoria when they received cocaine along with this experimental compound. Not surprisingly, the dopamine D1 receptor sites are located in the limbic system of the brain, where the brain's reward system is thought to be located. Research evidence suggests that cocaine also activates the opioid mu and kappa receptor sites, possibly as an indirect result of its ability to activate the dopamine D1 receptors.

Habitual cocaine misuse is thought to cause long-term changes in the activity of compounds in the brain such as ΔFosB ⁸ (Nestler, 2005), as well as the serotonin and norepinephrine neurotransmitter systems, although the significance of this effect is not known at this time (Acosta, Haller, & Schnoll, 2005; Reynolds & Bada, 2003). Cocaine also alters the function of a protein known as *postsynaptic density-95* (Sanna & Koob, 2004). Long-term changes in this protein, which is involved in the process of helping the synaptic junction between neurons adjust to changes in neurotransmitter density, are also thought to be involved in the process of learning and memory formation. This is thought to be one reason why individuals who misuse cocaine form such intense memories of their cocaine use, and why the relapse rate among individuals who are newly abstinent from cocaine is so high (Acosta et al., 2005; Sanna & Koob, 2004).

Although it is misused for its euphoric effects, tolerance to cocaine-induced euphoria develops very rapidly (Schuckit, 2006a). To counteract this tolerance, the individual may (a) increase the amount of cocaine used to the point where it may be lethal to the drug-naïve individual, or (b) inject small amounts of additional cocaine 2–3 times an hour after the initial euphoria begins to wear off. The ever-increasing dosage level of cocaine interferes with the normal function of the region of the brain known as the diencephalon, which helps to regulate body temperature. At the same time, the cocaine will cause the surface blood

vessels to constrict, making it harder for the body to cool itself. These effects can result in cocaine-induced **hyperthermia**,⁹ which is potentially life-threatening as the individual's body attempts to retain body heat at the very time that it needs to release it (Gold & Jacobs, 2005; Jaffe, Rawson, & Ling, 2005; Mendelson & Mello, 2008).

Drug Interactions Involving Cocaine

There has been remarkably little research into cocaine–pharmaceutical interactions (Karch, 2009). It is known that individuals who misuse cocaine often turn to other chemicals as a way to control the unwanted side effects of their cocaine use (Mendelson & Mello, 2008). For example, more than 62–90% of individuals who use cocaine have a concurrent alcohol use disorder (Gold & Jacobs, 2005). The use of cocaine during alcohol intoxication can alter the pharmacokinetics of both compounds. Scientists have observed a 30% increase in the blood plasma levels of cocaine in persons who use alcohol and cocaine simultaneously, as the alcohol interferes with the ability of the liver to biotransform the cocaine. Further, a small amount (<10%) of the cocaine in the individual's body will be transformed into **cocaethylene** (Karch, 2009; Repetto & Gold, 2005). Cocaethylene is a toxic compound that is thought to be 25–30 times as likely to induce death as cocaine (Karan, Haller, & Schnoll, 1998). Cocaethylene is thought to function as a calcium channel blocking agent in the heart, and has a biological half-life that is five times longer than that of cocaine alone, factors that are thought to increase the individual's risk of sudden cardiac death 18-fold as compared to that of an individual who does not use cocaine (Acosta et al., 2005; Hahn & Hoffman, 2001; Repetto & Gold, 2005). The concurrent use of alcohol and cocaine has also been identified as an element in the development of a potentially fatal pulmonary edema (Ciraulo, Shader, Greenblatt, & Creelman, 2006). Unfortunately, cocaethylene may extend the period of cocaine-induced euphoria, possibly by blocking dopamine reuptake, which acts as an incentive for the individual to continue to co-administer these compounds in spite of these dangers.

It is not uncommon for individuals who use cocaine to use cocaine and a narcotic analgesic simultaneously (a practice known as **speedballing**). For reasons that are not well understood, cocaine appears to enhance the respiratory depressive effects of the narcotic analgesics, possibly contributing to potentially fatal respiratory arrest. Further, as will be discussed later in this chapter, cocaine can induce feelings of irritation or anxiety, feelings that the individual

⁷It is interesting to note that Sukel (2012) reviewed research that suggested more activity in the nucleus accumbens of female rat mothers in response to exposure to their pups than to cocaine.

⁸See Glossary.

⁹See Glossary.

often attempts to control through alcohol, sedating agents, and/or marijuana. There is evidence that patients taking disulfiram as part of a treatment program for alcoholism achieve higher blood levels when they take cocaine, and this combination appears to cause a higher heart rate than when the person uses just cocaine (Karch, 2009). There is also evidence that persons taking antiviral medications may achieve higher blood concentrations of cocaine as the two compounds compete for biotransformation through the same metabolic pathway in the liver. While this list is not comprehensive, it does illustrate the fact that cocaine can interact with many other drugs that are misused or medications.

How Illicit Cocaine Is Produced

The production of illicit cocaine has changed little over the past decades. First, the cocaine leaves are harvested, a procedure that in some parts of South America might be done as often as once every 3–4 months. The collected leaves are dried in the open sunlight for a few hours to a few days. Although this is technically illegal, some local authorities are quite tolerant and do little to interfere with this process for the most part. Then the dried leaves are placed in a pit lined with plastic and mixed with water and sulfuric acid (White, 1989). The leaves are then crushed by workers who wade into the pit in their bare feet, stomping the mixture, from time to time, draining off the liquids. Lime is mixed with the residue, which then forms a paste, which is called “cocaine base.” It takes 500 kilograms of leaves to produce just one kilogram of cocaine base (White, 1989).

Next, compounds like water, gasoline, acid, potassium permanganate, and ammonia are added to the cocaine paste. This forms a reddish-brown liquid that is then mixed with a few drops of ammonia. This produces a milky solid, which is dried and then dissolved in a solution of hydrochloric acid and acetone, forming small particles that settle to the bottom of the tank. This is cocaine hydrochloride, which is filtered and dried under heating lights and then packed and shipped, usually in kilogram packages. As the cocaine moves through the distribution network, it is usually repeatedly adulterated, increasing its bulk and thus the profits for the dealer at each level of the distribution process.

Methods of Cocaine Misuse

Cocaine is misused in a number of ways. First, cocaine hydrochloride powder might be inhaled through the nose (intranasal use, or snorting, technically known as “insufflation”). It may also be injected directly into a vein. Cocaine

hydrochloride is a water-soluble compound, and thus is well adapted to both intranasal and intravenous use. Cocaine base might be smoked, and the fumes then rapidly gain access to the circulation for transport to the brain. Finally, cocaine might be administered sublingually (under the tongue), where the blood-rich tissues allow it to gain access to the circulation as it is absorbed. Each method of administration, while offering advantages to the individual using the cocaine, also exposes the person to potentially toxic levels of cocaine in spite of the assertion by drug dealers that they are “safe” (Repetto & Gold, 2005).

Insufflation

In 1903, the first case reports of cocaine-induced septal perforation began to appear in medical journals, suggesting that the practice of snorting cocaine is at least a century old (Karch, 2009). Those who snort cocaine arrange the powder on a piece of glass (such as a mirror), usually in thin lines of $\frac{1}{2}$ to 2 inches long and about one-eighth of an inch wide (Acosta et al., 2005). One gram of cocaine will usually yield around 30 such “lines” of cocaine (Acosta et al., 2005). The powder is diced up, usually with a razor blade, to enhance absorption. The powder is then inhaled through a tube such as a drinking straw or rolled-up paper, depositing the powder on the blood-rich tissues of the sinus membranes. About 60% of the cocaine deposited in the nasal passages is rapidly absorbed, with the first cocaine reaching the general circulation in 30–90 seconds, and it is then rapidly transported to the brain. The physical sensations reach peak intensity about 15–30 minutes after insufflation and begin to wear off in about 45–60 minutes following a single dose (Kosten & Sofuoglu, 2004). With repeated administrations, the peak effects might last twice as long as this (Hoffman & Hollander, 1997).

Because cocaine is a potent vasoconstrictor, it limits its own absorption through the nasal mucosa; thus, only 60% of the cocaine deposited into the nasal passages is absorbed (Gold & Jacobs, 2005). Then, 70–80% of the cocaine absorbed through the nasal passages is biotransformed by the liver *before* it is able to reach the brain, limiting the intensity of cocaine-induced euphoria experienced by the individual. These limiting factors make the inhalation of cocaine an ineffective means of cocaine misuse, and thus it is usually only seen in individuals who are casual or inexperienced users of cocaine.

Intravenous Cocaine Administration

It is possible to mix cocaine hydrochloride powder with water and then inject it directly into a vein. Intravenously administered cocaine will reach the brain in under 30 seconds

(Kosten & Sofuoglu, 2004), with virtually all of the injected cocaine being absorbed into the user's body (Acosta et al., 2005). While this allows for the rapid introduction of cocaine into the individual's body, it does not allow the individual to titrate the dose for optimal effect, and this may cause unwanted agitation. However, it is an effective way to achieve the "rush" or "flash" experience so desired by those who use intravenous cocaine (discussed later in this chapter).

Sublingual Cocaine Misuse

Cocaine hydrochloride powder is well adapted for absorption through the blood-rich tissues of the mouth, where it is rapidly absorbed and then transported to the brain in a manner similar to that seen with intranasal cocaine use. This method of cocaine misuse has not been studied in detail, although theoretically, an unknown percentage of the cocaine that is absorbed will be subjected to the first-pass metabolism effect. It is not known what percentage of the cocaine that is absorbed will ultimately reach the brain.

Rectal Cocaine Misuse

Rectal use of stimulants is popular among certain groups, such as men who have sex with men (Bourne & Weatherburn, 2017; Karch, 2009). Cocaine's local anesthetic properties provide some degree of relief from what would otherwise be painful forms of sexual activity. Unfortunately, the anesthetic properties of cocaine might also mask the pain signals that would warn the individual of physical trauma to the tissues of the rectal area, increasing the individual's risk for infection and possible death (Karch, 2009).

Cocaine Smoking

Historical evidence would suggest that the practice of burning, or smoking, different parts of the coca plant dates back to at least 3000 B.C.E., when the Incas would burn leaves at religious festivals (Hahn & Hoffman, 2001). The practice of smoking cocaine resurfaced in the late 1800s, when coca cigarettes were used to treat hay fever and opiate addiction. By the year 1890, cocaine smoke was being used in the United States for the treatment of whooping cough, bronchitis, asthma, and a range of other conditions. But while the practice of cocaine smoking for medicinal reasons dates back for more than a century, *recreational* cocaine smoking did not become popular until the mid-1980s.

While cocaine hydrochloride was a popular drug to misuse in the 1970s and 1980s, those using cocaine discovered that it could not easily be smoked. It had to be transformed back into the cocaine base ("freebase" or "base") through

a complex, labor-intensive process that involved the use of potentially explosive compounds. The mixture obtained was then passed through a filter in an attempt to remove as many impurities as possible, then smoked, inducing a sense of intense pleasure. Between 70 and 90% of the cocaine enters the circulation from the lungs when it is smoked, reaching the brain in as little as 7 seconds (Hahn & Hoffman, 2001; Mendelson & Mello, 2008). However, the risk of fire and/or explosion inherent in transforming cocaine back into coca base limited its popularity in the United States. To solve this problem, illicit distributors introduced a form of cocaine base that was already prepared for smoking: "crack." This form of cocaine is called crack because of the sound that it makes when smoked (Schuckit, 2006a).

Crack is essentially a solid chunk of cocaine base designed to be smoked, prepared as such before sale at the local level. This was done in illicit "factories" or "laboratories," which produce small, ready-to-use pellets that allow one or two inhalations. This form of cocaine for smoking has almost entirely replaced freebase cocaine in the United States (Karch, 2009). Although it would appear to be less expensive than cocaine prepared for intravenous injection, in reality, crack is about as expensive on a per-gram basis (Karch, 2009). Further, in spite of its reputation in some quarters as being safer than intravenously administered cocaine, it shares the same dangers as those found in cocaine injection.

On rare occasions, individuals who use intravenous cocaine have been known to attempt to dissolve pellets of crack in alcohol, lemon juice, vinegar, or water, and inject the resulting mixture (Acosta et al., 2005). This is usually done by those who are unable to obtain the desired cocaine hydrochloride for injection.

Gastrointestinal Absorption

It is possible to absorb cocaine through the gastrointestinal tract. If the person were to be a **body packer**¹⁰ and one of the packets were to rupture, the individual will absorb a massive cocaine overdose, usually resulting in the death of the individual (Esterson, Patel, Nicastro, & Friedman, 2017; Karch, 2009). Coca tea (commonly used in South America) will also allow the individual to absorb significant amounts of cocaine if too much is consumed. This can cause the individual to test positive for cocaine and its metabolites on urine toxicology testing, and thus the use of tea made from coca leaves should be avoided by those persons subject to urine toxicology testing (Karch, 2009).

¹⁰See Glossary.

Subjective Effects of Misused Cocaine

There are several factors that influence the individual's subjective experience of cocaine misuse. First are the individual's *expectations* for the compound's effects. Memories of past episodes of cocaine misuse both help to shape the individual's expectations for the drug's effects and trigger memories of past cocaine misuse that then contribute to the urge for the individual to engage in its use again (Gold & Jacobs, 2005). The actual *dose being used* is also a factor, although this is often difficult to estimate because of differences in the purity of cocaine sold in different locations. Finally, the *physiological effects* of the chemical help to shape how it is used. For example, individuals who smoke cocaine are able to stop smoking it when the side effects become uncomfortable.

Low blood levels of cocaine tend to cause an increase in the individual's libido, a feeling of increased energy, and a generalized feeling of arousal. At higher blood levels, such as those achieved through smoked or intravenously administered cocaine, will induce a sense of intense euphoria, known as the "flash" or the "rush," within seconds of the time that the drug is introduced into the body (Jaffe, Rawson & Ling, 2005; Stahl, 2008). This experience has been compared to sexual orgasm in intensity, and some males who misuse cocaine have reported spontaneous ejaculation without direct genital stimulation as a result of cocaine injection or smoking. Within a few seconds, the rush fades into a feeling of excitation or euphoria that lasts for 10–20 minutes.

Tolerance to the euphoric effects of cocaine develops rapidly. Individuals who misuse cocaine have developed several methods to overcome this tolerance. Some switch from cocaine snorting to smoking or injection. Others attempt to overpower cocaine-induced tolerance by engaging in extended periods of continuous cocaine misuse known as the "**coke run**." Cocaine "runs" last between 12 hours and 7 days, during which time the individual will inject additional cocaine perhaps as often as 2–3 times an hour until the cumulative dose reaches levels that would kill the cocaine-naïve individual (Mendelson & Mello, 2008). At the end of the coke run, the individual may fall into a prolonged sleep that may last for hours, or even days, and might experience a profound, possibly suicidal level of depression that slowly resolves as the brain's dopamine levels return to normal. Women have been shown to develop tolerance more quickly than males, often suffering more severe complications (Calipari et al., 2017). The consequences of cocaine misuse will be explored next.

Complications of Cocaine Misuse and Cocaine Use Disorder

Death

Cocaine use is a factor in between 40 and 50% of all deaths associated with illicit drug use (Karch, 2009). One possible explanation for this fact is that its use can exacerbate medical conditions that were present, even if only in subclinical forms (Mendelson & Mello, 2008). In some cases, the individual's death occurs so rapidly that s/he does not have a chance to reach a hospital, and the coroner is the only physician who will see the victim. In 2014, cocaine accounted for approximately 12% of all overdose deaths, an increase of almost 7% in 15 years (Ruhm, 2017). Recently, deaths related to cocaine in conjunction with opioids have also seen an increase, given the increase in heroin and fentanyl use (McCall Jones, Baldwin, & Compton, 2017). In addition to simply killing the individual, cocaine use can induce a wide range of other complications, discussed in the sections below.

Addiction

It was believed in the 1960s and 1970s that cocaine was not physically addictive, a misperception brought on by the fact that cocaine was so expensive and so difficult to find during that era that few individuals could afford to use it long enough to become addicted. With the availability of cheaper, more potent¹¹ cocaine, it has been discovered that cocaine addiction is not only possible, but that it may develop more rapidly than addiction to other compounds such as alcohol or marijuana. The addiction potential of cocaine might best be illustrated by the observation that a monkey would spend hours pushing a lever until he or she had pushed it 6,000 times, just to get a shot of cocaine (Rasmussen, 2008).

Cocaine is often portrayed as a universally addictive substance; in reality, only about 6% of those who begin to misuse cocaine will become physically addicted to it within the first year (Carroll & Ball, 2005).¹² If the individual continues to misuse cocaine, the percentage who become physically addicted increases until eventually 15% of those who initiated the use of cocaine will end up becoming addicted to it (Carroll & Ball, 2005; Jaffe, Rawson, & Ling, 2005).

¹¹As compared to what it cost in the 1960s and early 1970s.

¹²If only because it is not possible to predict which individuals are in danger of becoming addicted to cocaine and which persons are unlikely to become addicted to it, experimentation with cocaine is not recommended.

Respiratory System Problems

Individuals who smoke cocaine experience side effects such as chest pain, coughing, and damage to the bronchioles of the lungs (Gold & Jacobs, 2005; Jones & Weir, 2005). Approximately one-third of individuals who habitually use crack develop wheezing sounds when they breathe, and many experience an asthma-like condition known as chronic bronchiolitis (“**crack lung**”). It has been suggested that this might be due, at least in part, to contaminants in the cocaine that is smoked (Mendelson & Mello, 2008), and it is potentially deadly (Soni, Siddiqui, & Puttagunta, 2017). Other risks to smoking cocaine are the development of hemorrhage, pneumonia, and a chronic inflammation of the throat. On occasion, the individual who smokes cocaine will experience a situation in which the alveoli of the lungs will rupture, allowing the escape of air (and bacteria) into the surrounding tissues, known as a “**pneumothorax**,” establishing the potential for an infection to develop as well as compromising the ability of the smoker’s lungs to function properly. There is evidence suggesting that cocaine-induced lung damage may be permanent.

Cocaine smoking appears to be associated with an observed increase in the number of fatal asthma cases (“Asthma deaths blamed on cocaine use,” 1997). Individuals who snort cocaine chronically, called “snorters,” experience sore throats, inflamed sinuses, bleeding from the sinuses, hoarseness, and on occasion a breakdown in the cartilage in the nose, which can develop after just a few weeks of intranasal cocaine use (Karch, 2009). It is also common for those who use intranasal cocaine to experience the development of ulcers in the nasal passages, as cocaine-induced vasoconstriction and the impurities in illicit cocaine contribute to bacterial infections in these tissues.

Cardiovascular System Damage

The first report of a cocaine-related heart attack in the clinical literature was in 1886 (Gorelick, 2009). Cocaine use injures the heart through a variety of mechanisms. Cocaine misuse appears to be a major risk factor contributing to the buildup of plaque in the coronary arteries of individuals who use cocaine and who are between the ages of 18 and 45 (Karch, 2009; Lai et al., 2005; Levis & Garmel, 2005; McCord et al., 2008; Talarico et al., 2017). If the individual is also infected with HIV-1,¹³ the process of plaque buildup is accelerated (Lai et al., 2005). Repeated episodes of cocaine misuse seems to trigger the “complement cascade” normally seen when the body is invaded by foreign microorganisms.

The complement cascade allows the buildup of protein molecules on the cell walls of invading organisms, thus alerting the body’s **macrophages**¹⁴ to attack those cells. This would explain the theory that atherosclerotic plaque is formed when the macrophage cells mistakenly attack cholesterol molecules circulating in the blood and then attach these molecules to the endothelial cells of the coronary arteries. Over time, significant amounts of cholesterol accumulate, reducing the flow of blood through the vessel, contributing to the development of coronary artery disease.

For years, physicians were taught that cocaine-induced coronary artery spasms were the cause of the heart attacks so often seen in individuals who misuse cocaine. While such spasms do take place, they seem to play only a minor role in cocaine-induced heart attacks. Rather, cocaine misuse appears to first cause the buildup of coronary artery plaque where the endothelium has already been damaged, and then cause the coronary artery to constrict at these specific points during subsequent periods of abuse, reducing blood flow to the heart muscle. This process is also seen in cigarette smokers, although it does occasionally occur in nonsmokers as well (Jones & Weir, 2005). Patrizi et al. (2006) concluded that cocaine-induced coronary artery disease was the most common cause of myocardial infarctions in individuals who misuse cocaine, as evidenced by their finding that these individuals had significantly higher levels of atherosclerosis in their coronary arteries than did the individuals who did not use cocaine. It has been estimated that 25% of heart attack patients between the ages of 18 and 45 suffer at least one cocaine-related heart attack (Jones & Weir, 2005). So strong is the association between cocaine misuse and heart attacks that Tomb (2008) recommended that physicians assume that cocaine misuse was involved when a young adult experiences a heart attack until proven otherwise.

Fifty percent of individuals who use cocaine and who present at the hospital emergency room with heart pain have no evidence of atherosclerotic plaque buildup in their coronary arteries (Leamon et al., 2008). This does not negate the fact that cocaine is cardiotoxic; in addition to causing a heart attack, its misuse can result in severe hypertension, sudden dissection of the coronary arteries, cardiac ischemia, impaired platelet function, thrombosis, thromboembolism, tachycardia, micro-infarcts, myocarditis, cardiomyopathy, and sudden cardiac death (Bachi et al., 2017; Greenberg & Bernard, 2005; Jaffe, Rawson, & Ling, 2005; Karch, 2009; Mendelson & Mello, 2008; Stahl, 2008; Talarico et al., 2017). Cocaine can also potentially disrupt the normal electrical flow pattern in the heart, inducing potentially fatal

¹³Discussed in Chapter 36.

¹⁴See Glossary.

cardiac arrhythmias such as atrial fibrillation, sinus tachycardia, ventricular tachycardia, and the *torsade de pointes*¹⁵ (Gold & Jacobs, 2005; Karch, 2009; Khan, Morrow, & McCarron, 2009; O'Connor, Rusyniak, & Bruno, 2005). Fortunately, a small-scale study by et al., (2007) suggested that the compound dexmedetomidine might counteract many of cocaine's cardiovascular effects, offering the promise that physicians might soon have a new tool to protect the hearts of those foolish enough to use cocaine.

Some scientists believe that cocaine misuse causes *micro-infarcts*¹⁶ in the cardiac muscle (Aquaro et al., 2011; Gold & Jacobs, 2005). These micro-infarcts each slightly reduce the heart's ability to carry out its role as the circulatory system pump, and cumulatively may cause the individual's heart to fail. This theory is supported by the observation that individuals who misuse cocaine have abnormal electrocardiograms (EKG) in many cases, even if they are not actively using cocaine at the time of the test. These abnormal EKG tracings may reflect subclinical drug-induced heart damage, which will be exacerbated if the individual should continue to use cocaine. It is not known whether these micro-infarcts are the cause of the chest pain reported by some individuals who misuse cocaine, but it is known that cocaine misuse can induce areas of ischemia in body organs, especially the heart and brain.

There does not appear to be a specific pattern to cocaine-induced cardiac problems, and both individuals who use cocaine for the first time and those with a long history of prior cocaine misuse may both present with symptoms of a heart attack. Unfortunately, those who sell illicit drugs have been known to tell their clients that if the cocaine causes chest pain, it is a sign that the cocaine is very potent and not a sign of a possible cocaine-induced heart problem. If the individual should be hospitalized in the middle of an attack and fail to tell the physician that s/he had used cocaine, the physician might attempt to treat the suspected heart attack with medications such as the beta-adrenergic antagonists, which can exacerbate the cocaine-induced vasoconstriction and possibly kill the patient (Thompson, 2004).

A rare but potentially fatal complication seen with cocaine misuse is the *acute aortic dissection*, which might be caused by cocaine-induced episodes of hypertension (Karch, 2009; O'Brien, 2006; Westover & Nakonezny, 2010). Westover and Nakonezny (2010) suggested that 1.9% of the cases of aortic dissection reviewed were the result of cocaine misuse. This condition is a medical emergency and carries a

high mortality rate, even with surgical intervention. As the above information demonstrates, cocaine misuse carries with it a significant cardiovascular risk.

Cocaine Misuse as a Cause of Digestive System Damage

There is evidence that some of the metabolites of cocaine, especially cocaethylene, are quite toxic to the liver (Brust, 2004). However, the theory that cocaine misuse can directly cause or contribute to liver disease remains controversial (Karch, 2009). Still, some individuals have a genetic defect that prevents their bodies from producing an enzyme that plays a crucial role in cocaine biotransformation. This condition is called *pseudocholinesterase deficiency*, and persons with this condition are at risk for potentially fatal reactions to even small amounts of cocaine (Brust, 2004; Schuckit, 2006a). Additionally, cocaine use by those with HIV has been shown to increase risk of death, particularly as related to progression of liver disease (Campa et al., 2016).

Pancreatitis can also result from cocaine use (Chapela, de los Angeles Paz, & Ballesterro, 2017). On rare occasions, cocaine use can induce hemorrhage within the gastrointestinal tract, which might become so extensive that the individual expires in a short period of time from acute blood loss (Lingamfelter & Knight, 2010). Cocaine misuse has also been identified as a cause of bruxism, decreased gastric motility, perforation of the bowel, gangrene of the bowel, necrosis of the tissues of the esophagus,¹⁷ and ischemia to different regions of the intestinal tract. These later complications of cocaine misuse might become so severe that surgical intervention is necessary to remove the damaged portions of the intestinal tract.

Cocaine Misuse as a Cause of Central Nervous System Damage

Like the amphetamines, cocaine misuse causes a reduction in cerebral blood flow in at least 50% of those who use it (Balamuthusamy & Desai, 2006; Brust, 2004). Neuroimaging studies have found evidence of cerebral atrophy and enlarged ventricles within the brain, both indicators of the death of neural tissue (Bolla & Cadet, 2007; Lamarche, Cottet-Rousselle, Barret, & Fontaine, 2017). The observed changes in both the vasculature and structure of the brain might contribute to the lower cognitive functions seen in those who misuse cocaine. Researchers have found deficits in the areas of verbal learning, memory, and attention of

¹⁵See Glossary.

¹⁶Microscopic areas where the blood supply to cardiac tissue is disrupted, resulting in damage to the tissue supplied by those blood vessels.

¹⁷Clinically known as "*black esophagus*."

chronic cocaine abusers on neuropsychological test batteries (Kosten & Sofuoglu, 2004; Kosten, Sofuoglu, & Gardner, 2008). These neurocognitive deficits appear to continue for months after the individual's last cocaine use, and it is not known at this time whether they will resolve with extended abstinence (Gonzalez, Vassileva, & Scott, 2009).

Cocaine misuse is associated with an increased risk for either obstructive or hemorrhagic strokes (Bolla & Cadet, 2007; Chitsaz, 2017; Khan et al., 2009; Mendelson, Mello, Schuckit, & Segal, 2006; Westover, McBride, & Haley, 2007). These cocaine-induced strokes might be microscopic in size ("micro-strokes"), or they may involve major regions of the central nervous system. Kaufman et al. (1998) suggested that individuals who misuse cocaine were twice as likely as those who do not use cocaine the same age to suffer a stroke, while Johnson, Devous, Ruiz, and Alt-Daoud (2001) suggested that the risk might be as much as 14 times higher. There are no cocaine-specific areas of damage noted: Cocaine-related strokes have been identified in various regions of the brain, retina, and the spinal cord (Brust, 1997, 2004; Jaffe, Rawson, & Ling, 2005; Martin-Schild et al., 2010). The risk of suffering a cocaine-related stroke is apparently cumulative, with long-term use conferring higher risk than recently initiated use, although both groups are at risk for a cocaine-induced stroke. Individuals who misuse cocaine suffer a worse prognosis than those who do not use cocaine and are the same age, and tend to have larger areas of brain damage than those who do not use cocaine (Chang et al., 2013; Martin-Schild et al., 2010).

The causal mechanism for cocaine-induced strokes is thought to be the cycle of drug-induced vasospasm during periods of active drug misuse and the **reperfusion**¹⁸ that occurs in between these periods of cocaine use (Bolla & Cadet, 2007; Johnson et al., 2001; Karch, 2009). This can lead to damage to the blood vessel walls of the cerebral vasculature, facilitating the development of a stroke. Individuals who misuse cocaine are also at higher risk for *transient ischemic attacks* (TIAs) brought on as a result of their cocaine use, possibly because of cocaine-induced vasoconstriction (Kaufman et al., 1998).

Although the mechanism through which cocaine induces seizures remains unknown, cocaine is considered an **epileptogenic**¹⁹ compound, and the individual using cocaine is at increased risk for the development of seizures (Engel, 2013; Fadem, 2009; Gold & Jacobs, 2005; Mendelson & Mello, 2010). Even individuals using cocaine for the first

time might experience cocaine-related seizures (Gold & Jacobs, 2005). Physicians theorize that such seizures result from cocaine-induced interruptions in cerebral blood flow, substance-induced changes in the responsiveness of neurons in the brain to excitatory neurotransmitters, or a combination of these factors (Engel, 2013). There is also strong evidence that cocaine might initiate a neurological process known as **kindling**,²⁰ a phenomenon in which the individual's cocaine use lowers the seizure threshold, making future seizures more likely (Engel, 2013; Gold & Jacobs, 2005; Karch, 2009; Wilson, Shannon, & Shields, 2017). One region of the brain thought to be involved in the kindling process is the amygdala, although other regions of the brain might also be sensitive to cocaine use-related kindling.

Cocaine misuse is thought to interfere with the process of body temperature regulation, causing periods of *malignant hyperthermia* (Karch, 2009; Mendelson & Mello, 2010). The brain can only operate within a very narrow temperature range, and if the body temperature exceeds these limits, there is a very real danger of damage to the brain, if not even the death of the individual. There is also an emerging body of evidence that suggests that individuals who misuse cocaine are at high risk for alterations of the brain at the level of the individual neuron (Tannu, Mash, & Hemby, 2007). The authors compared samples of brain tissue from 10 cocaine overdose victims with those of persons who had died from non-cocaine-related causes. They found alterations in the expression of 50 different proteins involved in the process of forming and/or maintaining neural connections in neurons in the nucleus accumbens. Further research indicates that nucleus accumbens volumes seem to be reduced in individuals who use crack-cocaine, as opposed to those individuals who do not use (Schuch et al., 2017).

Habitual cocaine misuse has been implicated in the death of neurons, possibly because cocaine misuse alters the normal function of the *synuclein* family of proteins in the brain. Under normal conditions, these proteins help to regulate dopamine transport within the neurons. Some evidence suggests that chronic cocaine use can alter the process of synuclein production within the neuron, ultimately causing or contributing to the death of these neurons (Mash et al., 2003). Finally, there is also evidence suggesting that cocaine misuse may alter the blood-brain barrier,²¹ facilitating the entry of the human immunodeficiency virus type 1 (HIV-1)²² into the brain. Further, because of

¹⁸See Glossary.

¹⁹See Glossary.

²⁰See Glossary.

²¹Discussed in Chapter 3.

²²Discussed in Chapter 36.

the various bacterial, fungal, or viral contaminants in some samples of illicit cocaine, the individual using cocaine is being exposed to a number of potentially fatal infectious agents (Acosta et al., 2005). For example, the intranasal use of cocaine induces a state of intense vasoconstriction in the tissues of the sinuses. This might cause tissue death in the affected areas, establishing focal colonization points for bacteria resulting in sinusitis, loss of a sense of smell, nose bleeds, or even a potentially fatal brain abscess if the bacteria are able to access the brain through the nasal cavity (Roldan & Patel, 2008).

Cocaine's Effects on Emotions and Perceptions

It is not uncommon for individuals who misuse cocaine to report experiencing periods of depression or anxiety (Gorelick, 2009). Up to 64% of individuals surveyed who acknowledged cocaine use had experienced some degree of anxiety as a result of their cocaine use (Louie, 1990). Individuals who misuse cocaine may attempt to control this anxiety by concurrently using sedating agents such as marijuana, benzodiazepines, alcohol, narcotic analgesics, and, on occasion, barbiturates. Cocaine-related anxiety attacks might persist for months after the individual's last cocaine use (Gold & Jacobs, 2005; Schuckit, 2006a). Further, there is evidence that cocaine use might lower the threshold at which the individual will experience an anxiety attack (Gold & Jacobs, 2005).

Statistically, individuals who misuse cocaine are also at increased risk for premature death from suicide and homicide (Oehmichen, Auer, & Konig, 2005), especially when alcohol is used simultaneously with cocaine (Arias et al., 2016; Conner et al., 2017). Oehmichen and colleagues (2005) concluded that suicide accounted for 10% of deaths for those who use cocaine, while homicide accounted for another 20%.²³ There is a known relationship between cocaine withdrawal and depression, which is an independent risk factor for suicide. Further, cocaine misuse can exacerbate symptoms of both **Tourette's syndrome** and **tardive dyskinesia** (Lopez & Jeste, 1997). After extended periods of misuse, some individuals develop the sensation of having bugs crawling on, or just under, their skin. These hallucinations are known as **formication**,²⁴ and those who misuse cocaine have been known to scratch, burn, or cut themselves

in an attempt to relieve themselves of the torment of these nonexistent insects (Gold & Jacobs, 2005).

Cocaine misuse has also been identified as the cause of a drug-induced psychosis (Areal, Herlinger, Pelição, Martins-Sylva & Pires, 2017; Schuckit, 2006a). A significant percentage of individuals who use cocaine on a chronic basis will exhibit symptoms of a psychosis that are very similar to those seen in paranoid schizophrenia. This condition, known as "**coke paranoia**" by individuals who misuse cocaine, usually clears within a few hours or days of the individual's last cocaine use (Haney, 2004; Karch, 2009; Schuckit, 2006a; Stahl, 2008). The mechanism through which extended periods of cocaine misuse is able to cause a drug-induced psychosis is not known, and further research is needed into this phenomenon.

Other Problems Associated with Cocaine Misuse

Men who misuse cocaine run the risk of developing erectile dysfunctions, including a painful, potentially dangerous condition known as **priapism**²⁵ (Karch, 2009). Further, as noted earlier in this chapter, the rectal use of cocaine may, although it reduces the individual's awareness of pain, contribute to tissue damage, development of infection, and possible death. Cocaine has been implicated as a cause of death through the potentially fatal condition known as **rhabdomyolysis**²⁶ (Khan et al., 2009; Nanavati & Herlitz, 2017; Schuckit, 2006a). Rhabdomyolysis is thought to be the result of cocaine-induced vasoconstriction, causing ischemia in the muscle tissue (Karch, 2009; Repetto & Gold, 2005; Richards, 2000). Cocaine is also known to cause **choreoathetoid movement** in some individuals, which is "uncontrolled writhing movements secondary to excess dopamine," which is also frequently called "**crack dancing**" (Doobay, Sun, Shah, Masuta, & Shepherd, 2017, p. 1).

Cocaine Withdrawal

A few hours after the individual last snorts cocaine, or within 15 minutes of the last intravenous or smoked dose, the individual will slide into a state of deep depression, which could reach suicidal proportions (Gold & Jacobs, 2005). This depressive effect is thought to reflect the cocaine-induced depletion of the neurotransmitters dopamine and norepinephrine in the brain. After a period of abstinence, the

²³Cocaine-induced heart disease, infections (including HIV-1), strokes, and accidents accounted for the other 70% of those individuals who used cocaine and who died.

²⁴See Glossary.

²⁵See Glossary.

²⁶See Glossary.

neurotransmitter levels slowly return to normal. But there is a possibility that the individual's cocaine use masked a pre-existing depressive disorder that will only become apparent after the individual discontinues the use of cocaine.

Other symptoms frequently seen during cocaine withdrawal include: fatigue, vivid and intense dreams, sleep disorders (both insomnia and hypersomnia), anorexia, and psychomotor agitation or retardation (Carroll & Ball, 2005). Many individuals who use cocaine report experiencing cognitive problems upon cessation, which may continue for 6 months or longer (Morgan et al., 2006). There is evidence to suggest that individuals who use cocaine are less likely than individuals who use other illicit compounds to report insomnia when they discontinue the use of cocaine, yet they may actually be sleeping less than they expect (Hodges, Pittman, & Morgan, 2017; Morgan et al., 2006). This sleep disturbance, called **occult insomnia**, has been shown to be related to the possibility of relapse (Hodges et al., 2017; Morgan et al., 2006).

CNS Stimulant Misuse and the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

The discussion of cocaine-related disorders under the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013) involved one topic heading: the *stimulant use disorders*, which was presented in the last chapter. To follow the same outline used by the American Psychiatric Association, this discussion is found at the end of Chapter 8.

Chapter Summary

It is often surprising for students to learn that cocaine is nothing more than a natural pesticide produced by the coca plant in an attempt to ward off insects or animals that might otherwise consume the leaves of the plant. By coincidence, this compound also has a strong impact on the central nervous system (CNS). Early settlers in the high Andes mountain regions found that by chewing the cocaine leaf, they could enhance their endurance while working at these high altitudes. It soon became a valued part of the culture prior to the arrival of European explorers.

With the development of methods to chemically extract cocaine from the leaf and concentrate it, and the almost simultaneous development of the hypodermic needle, the world entered a new era of cocaine use. It was found that if concentrated, smoked, or injected that it could induce a powerful sense of euphoria that is, at least in the opinion of some individuals, "better than sex." This soon made cocaine the stimulant of choice for many. Over time, it was discovered that while cocaine might indeed make the individual feel good, it also contributed to a wide range of potentially lethal problems, and individuals who sought out illicit drugs drifted away from cocaine use to the supposedly safer pleasures of the amphetamines in the 1930s. By the 1960s or 1970s, they had discovered that these compounds were dangerous, but the lessons so painfully learned by those who misused cocaine at the turn of the 20th century had been forgotten. Cocaine again became a major drug to misuse, and the dangers associated with its use were rediscovered. It remains a significant component of the drug use problem in the United States in spite of the known dangers associated with its use.



CHAPTER 10

Marijuana Use and Misuse¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 10.1** Understand the history of marijuana
 - 10.2** Describe the issues related to potency of marijuana
 - 10.3** Describe the scope of the problem of marijuana use and misuse
 - 10.4** Comprehend the pharmacology, methods of use, and subjective effects of marijuana
 - 10.5** Describe the adverse effects and consequences of chronic marijuana misuse
 - 10.6** Understand the DSM criteria for cannabis-related disorders
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Introduction

Although the exact age of the Chinese manuscript is disputed, current evidence would suggest that the earliest written reference to marijuana as a medicine dates back to 2727 B.C.E. (Grinspoon, Bakalar, & Russo, 2005), and there is evidence of its use for other purposes dating back more than 6,000 years (Kelly & Levin, 2015). Currently, it is a rather controversial substance, legally available in a number of states, and sold by prescription in a number of others. Preliminary evidence suggests that since its legalization, the number of persons with a cannabis use disorder (CUD) has doubled, and illicit use has increased more in states which have legalized medical use, as has CUD (Hasin et al., 2015, 2017). This data is sure to add to the controversy surrounding its legal status and use.

It remains a subject of controversy, sparks fierce debate, and it has been the source of many “urban myths,” not the least of which is that marijuana itself is a drug rather than a plant. It is a member of the *Cannabis sativa* family, which has long been known and used by humans. Indeed, the very name *Cannabis sativa* is Latin for “cultivated hemp” (Green, 2002). Historical evidence suggests that some varieties of the cannabis plant have been cultivated for hemp fiber for over 12,000 years (Welch, 2009). The hemp fibers are then used to manufacture a

¹The topic of “medical” marijuana is discussed in Chapter 38.

variety of products,² the range of which will often surprise the student.

In the United States, the topic of marijuana has reached such a point of hysteria that *any* member of the *Cannabis sativa* family of plants is automatically assumed to have a major misuse potential (Williams, 2000). This is hardly the truth, for some varieties produce hemp *fiber*, which has little or no misuse potential, while others are bred to produce large amounts of those compounds that give marijuana a psychoactive effect. To differentiate between these two plant varieties, Williams (2000) suggested that the term **hemp** be applied to those plants grown for their ability to produce fiber, while the term **marijuana** be reserved for just those members of the *Cannabis sativa* family grown for their ability to produce compounds with a psychoactive effect. This is the convention that will be followed in this text as we explore the problem of marijuana use and misuse.

A History of Marijuana Use/Misuse

Almost 3,000 years ago, physicians in China were using marijuana as a treatment for malaria and constipation, to ease the pain of childbirth, and, when mixed with wine, a surgical anesthetic (Robson, 2001). In the United States, historical evidence suggests that the settlers in Jamestown, Virginia, began to harvest cannabis for its ability to produce hemp fibers in 1611, fibers that, among other uses, were used to produce rope for the sailing ships of the era (Grinspoon et al., 2005). Its intoxicating effects have been known at least since the 1800s, although there is evidence that in Central and South America people may have used marijuana for its intoxicating effects even before this time (Grinspoon et al., 2005). Physicians in Asia, Europe, and the New World viewed cannabis/marijuana as a treatment for a wide variety of disorders. In the United States, for example, physicians were trained to prescribe marijuana as a sedative, a hypnotic, a treatment for migraine headaches, and an anticonvulsant. By the turn of the 20th century, no less a company than Sears, Roebuck, and Company sold marijuana as a cure for the then-prevalent morphine addiction (Brust, 2004).

²For example, clothing has been made from hemp for thousands of years. The King James translation of the Bible was printed on paper manufactured from hemp. Both Rembrandt and van Gogh painted on “canvas” made from hemp (Williams, 2000). While George Washington cultivated cannabis to obtain hemp, which was used to manufacture rope and other products during the era, there is no direct evidence that he ever smoked marijuana.

Anecdotal Claims of Efficacy

For more than half a century, physicians have offered anecdotal evidence suggesting that marijuana, or at least a compound including marijuana, could be useful in treating one or more diseases that continue to plague mankind. Case reports surfaced in the 1970s that cancer chemotherapy patients reported having less nausea after smoking marijuana (Robson, 2001). These case reports resulted in the development of the synthetic drug Marinol® (dronabinol), which is concentrated Δ -9-tetrahydro-cannabinol (THC).³ This compound has met with only limited success in controlling chemotherapy-related nausea, and it has been suggested that at higher doses, dronabinol and similar compounds have the same psychoactive effect as smoked marijuana (Schatman, 2015). However, reviews of evidence to date do indicate strong evidence for the use of forms of medical marijuana to lessen nausea and vomiting in chemotherapy patients (National Academies, 2017). Anecdotal reports also indicate that marijuana provides symptomatic relief from the discomfort of a range of gastrointestinal disorders (Gerich, Isfort, Brimhall, & Siegel, 2015), which does suggest a need for objective research into the possibility that a chemical or chemicals found in marijuana would be of value as a new pharmaceutical for treating gastrointestinal discomfort.

Individuals with multiple sclerosis (MS) have often reported improved functioning after smoking marijuana.⁴ This was consistent with the results of the research by Zajicek and colleagues (2012), who found that concentrated THC appears to reduce muscle stiffness in a subgroup of persons struggling with MS. Such reports supported the introduction of Sativex®, a pharmaceutical now in use in other countries but not currently available in the United States. Sativex is sprayed under the tongue, where the concentration of blood vessels aids in its rapid absorption as an aid to the treatment of multiple sclerosis (Wilson, 2005). Review of the evidence to date does suggest the marijuana can be helpful with MS and potentially with sleep-related issues related to MS (National Academies, 2017).

In the Netherlands, early research suggested that marijuana use could ease the symptoms of neurological disorders, pain, and help reverse the “wasting syndrome” so often seen

³The compound thought to be the primary psychoactive agent in marijuana.

⁴However, Papathanasopoulos, Messinis, Epameinondas, Kastellakis, and Panagis (2008) did question whether cannabinoids might also induce changes in brain function that would contribute to cognitive decline in patients with MS, and the final answer to the question of whether cannabis should play a role in the treatment of MS remains open to debate.

in cancer and AIDS patients (Gorter, Butorac, Coblan, & van der Sluis, 2005; Villarreal, 2011). The Health and Medicine Division of the National Academies of Science (2017) does indicate strong evidence for the use of medical marijuana for chronic pain as well as some evidence for use with sleep issues related to chronic pain.

Other researchers have found evidence suggesting that at least one of the compounds in marijuana smoke might be of possible value in treating Alzheimer's disease (Eubanks et al., 2006; Horstman, 2010). There is also limited evidence suggesting that a compound in marijuana might have at least a short-term beneficial effect for patients with amyotrophic lateral sclerosis (ALS) (Amtmann, Weydt, Johnson, Jensen, & Carter, 2004). Further, there is a growing body of evidence that one or more of the compounds in marijuana might reduce neuropathic pain, such as that associated with HIV-1 infection (Abrams et al., 2007; Villarreal, 2011).

An illustration of the scientific debate surrounding marijuana are studies based on animal research suggesting that one or more compounds in marijuana appear to function as potent antioxidants, possibly proving of value in limiting the amount of damage caused by a stroke or neurological trauma (Hampson et al., 2002; Papathanasopoulous et al., 2008). Other evidence suggests that marijuana use might *increase* the risk of suffering a stroke, raising questions as to whether marijuana would be of value in treating neurological trauma or whether it is a potential causal agent for strokes (Mullen, 2016). Obviously, there is a need for more research on this topic.

Early research studies suggested that smoking marijuana might help control certain forms of otherwise unmanageable glaucoma; however, follow-up studies failed to replicate these findings (Green, 2002; Watson, Benson, & Joy, 2000). Further study is needed as current research indicates the ineffectiveness of medical marijuana for glaucoma (National Academies, 2017). Physicians have reason to believe that a compound in marijuana might prove to be useful in treating asthma, Crohn's disease, anorexia, emphysema, epilepsy, and possibly hypertension (Green, 2002; Seppa, 2010). There is also strong evidence that a compound in marijuana might inhibit tumor growth, including **gliomas**⁵ (Salazar et al., 2009; Seppa, 2010). Further in-depth study of possible medicinal uses for marijuana in the United States is needed.

A Question of Potency

Ever since it became a popular compound to misuse in the 1960s, those who use marijuana have sought ways to enhance its effects, either by intermixing the marijuana

with other compounds, or by obtaining strains with the highest possible concentration of those compounds thought to give marijuana its psychoactive effects. One such compound is **Δ -9-tetrahydro-cannabinol**⁶ (THC) (Coghlan, 2009). Over the years, there have been clandestine efforts to cross-breed marijuana plants with high levels of THC with other strains with high levels of THC to produce new strains with even higher levels of THC. These efforts have been successful. In 1992, the average concentration of THC in marijuana seized by police was 3.08%, which had increased to 5.11% by the year 2002 (Compton, Grant, Collier, Glantz, & Stinson, 2004) and averaged 9.6% by 2004 (Munsey, 2010; Office of National Drug Control Policy, 2008). There is evidence that the THC content of some strains of marijuana being sold today might be as high as 23–33% (Dujourdy & Besacier, 2017; Schatman, 2015).

Unfortunately, much of the research data on marijuana, its potential uses, misuses, and dangers was carried out 25 years ago, when less potent strains were commonly used, and thus there are questions as to its applicability at this time ("Potent pot," 2008). Further, scientists are only now learning more about the brain's endocannabinoid system and how THC alters the function of this system. Thus, the conclusions of much of the early research into the safety of marijuana, and anecdotal reports of its efficacy in treating different conditions, may no longer be applicable, and the consequences of using the higher potency strains of marijuana are not known at this time.

A Technical Point

Marijuana is not a drug: It is a plant, a member of the cannabis family of plants, and the strain known as *Cannabis sativa* is the strain of cannabis most commonly misused. It contains more than 400 different compounds, a number of which are psychoactive (Gold, Frost-Pineda, & Jacobs, 2004; Mendelson & Mello, 2008; Sadock, Sadock, & Ruiz, 2015). In the 1960s, researchers discovered that the majority of marijuana's effects are caused by a compound commonly known as THC.⁷ Individuals using marijuana ingest or smoke the marijuana plant to admit THC to their bodies. THC is found throughout the marijuana plant, but the highest concentrations are found in the small upper leaves and the flowering tops of the plant. Historically, the term *marijuana* is applied to preparations of the plant used for smoking or eating. **Hashish** is used to identify the thick resin that is

⁶Discussed elsewhere in this chapter.

⁷The chemical name of which is Δ -9-tetrahydro-cannabinol.

⁵See Glossary.

obtained from the flowers of the cannabis plant. This resin is dried, providing a brown or black substance that has a high concentration of THC. The resin is then either ingested orally (often mixed with a sweet substance to mask its flavor) or smoked. **Hash oil** is a liquid extract from the plant, usually containing 25–60% THC, which is added to marijuana or hashish to enhance its effect. *Cannabis* is the term often used to refer to medicinal marijuana, but it is also used to refer to the forms used for recreational purposes. In this chapter, the generic term *marijuana* will be used for any part of the plant that is to be smoked or ingested, except when the term *hashish* is specifically used.

Scope of the Problem

Marijuana has been the most commonly used illicit substance in the United States (Kelly & Levin, 2015; SAMHSA, 2106, 2017) and on this planet (Coghlan, 2009; Mullen, 2016; U.N. Office on Drugs and Crime, 2017). The United Nations reported that 182.5 million persons having used marijuana at least once in the past year. The United States is the largest market for marijuana (U.N. Office on Drugs and Crime, 2017), with 24 million people who use marijuana in a given month (up from 22.2 million the prior year), accounting for 8.9% of the population over age 11 (SAMHSA, 2016, 2017). Lifetime prevalence of marijuana use in the United States is around 44% of those over age 11, whereas use in the past year is around 13.5% (SAMHSA, 2016). It is expected that these numbers will continue to rise, given the move toward legalization of marijuana use across the country.

The estimated value of the annual marijuana plant harvest each year in the United States makes it *the* biggest cash crop raised in this country, generating more income than corn and wheat combined (“Grass is greener,” 2007; Stratton & Hill, 2010). In 2016, sales of legal marijuana reached \$6.7 billion in the United States (ArcView Market Research, 2017). The number of individuals who have used marijuana in the past or who currently use marijuana has been estimated to be just under 47% of persons age 18 and older, and each day approximately 6,000 more people in the United States use marijuana for the first time (Danovitch & Gorelick, 2012; Sadock et al., 2015; SAMHSA, 2016). The average age at which individuals begin to smoke marijuana in the United States is around the late teenage years into the early twenties (Ellickson, Martino, & Collins, 2004; Kelly & Levin, 2015). In earlier age cohorts, marijuana use peaked in the early adult years and then became less common during the individual’s twenties and thirties. For the current generation of young adults, marijuana use has been viewed as a normal recreational activity for all their lives (United Nations, 2011), and it is not clear whether this pattern of use will continue

or if younger generations will establish different behavioral norms for marijuana use.

There are parallels between marijuana misuse patterns and those of alcohol: Fourteen percent of those who smoke marijuana do so daily, consuming 95% of the marijuana sold on the illicit market in this country (United Nations, 2011). The other individuals who use marijuana engage in rare use, and only a small percentage of those who use marijuana use more than 10 grams a month (enough for about 25–35 cigarettes) (MacCoun & Reuter, 2001). In spite of its reputation as not being addictive, some individuals do develop a psychological dependency on it, and 10–20% of individuals who use marijuana will become physically addicted to it (Sadock et al., 2015). Approximately 4 million individuals in the United States had a cannabis use disorder in 2016 (SAMHSA, 2017).

Because of its popularity as a substance to misuse, older legal and social sanctions against marijuana use have repeatedly changed. In some states, possession of small amounts of marijuana for personal use is legal, in other states it is only subject to a fine, while in some states the possession of the same amount of marijuana would result in major legal sanctions.

The Pharmacology of Marijuana

In spite of its long history as a popular substance of misuse, and its even longer history as a folk medicine, the pharmacokinetics of marijuana are still not completely understood (Grinspoon et al., 2005). It is known that the *Cannabis sativa* plant contains at least 400 different compounds, of which 61 or more are psychoactive (Gold et al., 2004; Mendelson & Mello, 2008; Sadock et al., 2015; Welch, 2009). Of the 400 known compounds found in marijuana, at least 21 are under investigation as potential pharmaceuticals (Welch, 2009). The majority of marijuana’s psychoactive effects are thought to be caused by a compound known as Δ -9-tetrahydro-cannabinol⁸ (THC), although there is a possibility that some of the other psychoactive compounds in marijuana might contribute to its observed effects.

In addition to THC, a compound known as **cannabidiol (CBD)** is also inhaled when marijuana is smoked. Clinical research suggests that while it does not bind at known THC receptor sites, it does appear to modify the effects of THC through an unknown mechanism⁹ (Borgwardt et al., 2008; Schatman, 2015). The current strains of marijuana have an

⁸ Δ is the Greek letter Delta.

⁹There is also significant evidence suggesting that CBD might be the compound that makes marijuana potentially useful in the treatment of seizure disorders, have an anti-inflammatory effect, and might even be useful in the treatment of schizophrenia.

inverse relationship between THC and CBD: Those strains with high THC levels have low levels of CBD, and those strains of marijuana with low levels of THC seem to have higher levels of CBD.

There is no “standard” dose of marijuana, since the potency varies significantly between samples. Further, if it is smoked, intraindividual and interindividual variability in the smoking process can influence the amount of marijuana smoke reaching the lungs. Such factors as the number of “puffs,” time interval between puffs, depth of inhalation with each puff, and time that the individual holds their breath after inhaling marijuana smoke all influence the amount of THC that reaches the circulation. Once it reaches the circulation, THC is rapidly distributed to blood-rich organs such as the heart, lungs, and brain. Then, over time, it slowly works its way into less blood-rich tissues such as the body’s fat reserves, where THC is stored. For the individual who only uses marijuana rarely, this is not a matter of significant concern since the THC will be released back into the circulation and eliminated from the body within a few hours of the time the marijuana was smoked or ingested. Chronic misuse results in significant amounts of THC being stored in the body’s fat cells, and upon cessation it is slowly released back into the blood (McDowell, 2005).

In spite of strident claims to the contrary, individuals who use marijuana infrequently will usually only have marijuana metabolites in their urine for about 72–96 hours after their last use of this substance.¹⁰ About 65% of a single dose of marijuana is excreted in the feces and only 20% in the urine (Huestis, 2009). Individuals who use marijuana on a chronic basis might test positive for THC in their urine for up to 30 days, but this happens only with exceptionally heavy levels of marijuana use (Stephens & Roffman, 2005).

In the body, THC is biotransformed into a compound known as 11-hydroxy- Δ^9 -THC, and this metabolite is thought to cause marijuana’s psychoactive effects (Sadock et al., 2015). Between 97 and 99% of the THC that reaches the blood is protein-bound, so its immediate psychoactive effects are caused by the 1–3% that remains unbound (Huestis, 2009; Jenkins, 2007). When it is smoked, the peak blood levels are seen within 10 minutes, and THC blood levels drop to 10% of the peak level within 1 hour (Gonzalez, Vassileva, & Scott, 2009; Hall & Degenhardt, 2005). The absorption, distribution, biotransformation, and elimination of marijuana is slower when it is ingested orally, but after absorption from the gastrointestinal tract the THC is still protein-bound in the same pattern as noted above.

THC mimics the action of two and possibly more naturally occurring neurotransmitters in the brain, collectively called **endocannabinoids**¹¹ (Kelly & Levin, 2015; Kraft, 2006; Lovinger, 2008; Villarreal, 2011). Receptor sites for the endocannabinoids have been found throughout the brain, including the hippocampus, cerebral cortex, basal ganglia, cerebellum, and the dorsal horns of the spinal cord (Cruz, Bajo, Schweitzer, & Roberto, 2008; Gonzalez et al., 2009; Kelly & Levin, 2015; Martin, 2004; Nicoll & Alger, 2004; Welch, 2009; Zajicek et al., 2003). There are also receptor sites for endocannabinoids on immune cells, which indicates that they seem to be involved in immune responses as well as inflammation (Kelly & Levin, 2015). THC’s effects are thought to be between 4 and 20 times as potent as the endocannabinoids, and thus more likely to gain access to these receptor sites (Lovinger, 2008; Martin, 2004). Surprisingly, the endocannabinoid receptor site network matures during adolescence, a discovery that might have implications for substance rehabilitation workers who specialize in treating adolescents (Lewis, 2011).

The principal endocannabinoids that have been identified to date are the compounds *anandamide* and *sn-2 arachidonylglycerol* (or, simply, 2-AG) (Cruz et al., 2008), although additional endocannabinoids may exist (Kelly & Levin, 2015). Both of these compounds are synthesized in the body from lipid molecules, and since their discovery, they have emerged from obscurity to be recognized as essential components of normal bodily function. The anandamide receptors are involved in the regulation of mood, memory, cognition, perception, muscle coordination, regulation of sleep, body temperature regulation, appetite, pain perception, and possibly regulation of the immune system (Gruber & Pope, 2002; Martin, 2004; Nowak, 2004; Parrott, Morinan, Moss, & Scholey, 2004; Reynolds & Bada, 2003; Welch, 2009). Animal research suggests that anandamide also helps to guide the specialization of what are known as pyramidal cells in the brain and the pattern of axon growth in new neurons¹² (Berghuis et al., 2007; Fields, 2009; Lovinger, 2008; Mulder et al., 2008).

It would appear that CB1 is involved in cellular necrosis, marking diseased cells for destruction and absorption by the body. Anandamide also functions as a *retrograde neurotransmitter molecule*, which modulates the release of many neurotransmitters from one neuron to the next (Lovinger, 2008). This reduces the firing rate of the receptive neurons, which subjectively is experienced as a calming effect. Normally, this neurotransmitter inhibition continues

¹⁰Some individuals whose urine toxicology test is positive for THC claim that they had consumed a form of beer made from hemp. While creative, this claim has not been supported by research evidence.

¹¹A contraction of the term endogenous cannabinoids.

¹²A process known as **cortico genesis**, which is discussed in the Glossary.

for as long as the endocannabinoid molecules are present at the synaptic junction. Experimental research suggests that by blocking the endocannabinoid receptors, it is possible to reduce drug-seeking behaviors not only for marijuana, but also for food, nicotine, and possibly other drugs. These findings suggest new avenues of possible treatment for individuals with SUDs and possibly the eating disorders (Kraft, 2006; Le Foll & Goldberg, 2005; Mone, 2012).

The compound 2-AG is thought to be manufactured in the hippocampus region of the brain, and it appears to bind at the CB2 receptor site (Parrott et al., 2004). It was once thought that the CB2 receptor site was found exclusively in immune system, although emerging evidence suggests that there are at least a limited number of CB2 receptor sites in the hippocampus (Mone, 2012; Villarreal, 2011). This would appear to account for marijuana's ability to influence immune system activity. There is strong evidence that the endocannabinoids influence the development of cancer, including carcinoma of the lung, gliomas,¹³ some forms of throat and thyroid cancers, leukemia, cancer of the skin, cancer of the uterus, breast cancer, prostate cancer, bowel cancer, and neoblastoma (Lehne, 2013; Seppa, 2010). This is not to imply that 2-AG *causes* these forms of cancer, and there is evidence that at least one form of cancer—bowel cancer—develops only when 2-AG is absent or its action is suppressed by the evolving cancer.

All of these forms of cancer have a protein complex on the cancer cell's walls that forms the CB2 receptor site. When this receptor site is activated, a chemical cascade within the cell begins causing it to produce ceramide, a fatty molecule that induces cellular death (Seppa, 2010). At least some forms of cancer have learned to suppress or totally inactivate the action of 2-AG at these CB2 receptor sites, allowing the cancer to escape detection by the immune system. Another function of 2-AG appears to be helping to eliminate aversive memories (Cruz et al., 2008; Marsicano et al., 2002; Martin, 2004; Robbe et al., 2006). The available evidence would suggest that under normal conditions 2-AG interferes with the firing sequence of subunits of the hippocampus involved in normal memory formation, which may be related to the finding that those who use marijuana report having some memory problems. Data discovered by Riba and colleagues (2015) show that even a month after their last marijuana use their participants who used marijuana were more likely to report seeing words on a memorization task that participants in the non-using control group did not see, suggesting an increased

susceptibility to the formation of false memories even after achieving abstinence from marijuana use.

Marijuana has also been found to affect the synthesis of **acetylcholine**¹⁴ in the limbic system and cerebellum regions of the brain (Fortgang, 1999). This might be the mechanism by which marijuana causes the user to feel sedated and relaxed. Marijuana has also been found to have a mild analgesic effect, and is known to potentiate the analgesic effects of narcotic analgesics (Anand et al., 2008; Martin, 2004; Welch, 2009). Since the cannabinoids are involved in peripheral pain perception, it may be possible to develop drugs that will target this pain perception system without the intoxicating effects of marijuana (Anand et al., 2008). This effect appears to reflect marijuana-induced inhibition of the enzyme **adenylate cyclase**, which is involved in the process of transmission of pain messages in the CNS. Marijuana is also able to inhibit the production of **cyclooxygenase**,¹⁵ which is possibly another mechanism through which it is able to inhibit pain perception without the sedation seen when narcotic analgesics are used (Carvey, 1998; Whitten, 2008b). The analgesic effects of marijuana appear to peak about 5 hours after it was used (Welch, 2009). Scientists are not sure of the analgesic potential of marijuana, which was once thought to be about that of codeine, but they are exploring the possibility of adapting a compound found in marijuana as an analgesic (Welch, 2009).

The mechanism by which marijuana is able to induce a sense of mild euphoria is not fully understood. Like other drugs that are misused, marijuana's euphoric effects appear to reflect its effects on the brain's endogenous opioid neurotransmitter system (Welch, 2009). The primary site of THC biotransformation is in the liver, and more than 100 metabolites are produced during this process (Hart, 1997). The half-life of THC appears to depend on whether metabolic tolerance to its effects has developed. Even under the best of conditions, the body is not able to biotransform THC quickly, and in chronic abusers the half-life might vary from 24 to 96 hours (Oehmichen, Auer, & Konig, 2005). About 65% of THC metabolites are excreted in the feces, and the remainder is eliminated from the body in the urine (Hubbard, Franco, & Onaivi, 1999). Tolerance to the effects of THC develops rapidly (O'Brien, 2006; Welch, 2009). After the development of tolerance, the individual must either wait a few days before using marijuana again until the body begins to lose its tolerance to marijuana, or change the method by which s/he uses marijuana.

¹³See Glossary.

¹⁴See Glossary.

¹⁵See Glossary.

For example, those who use marijuana orally might switch to smoking marijuana, or those who smoke might switch to more potent varieties for smoking.

Interactions Between Marijuana and Other Chemicals

There has been relatively little research into potential interactions between marijuana and other compounds. Thus, there is a significant possibility that there are undiscovered interactions between marijuana and various pharmaceuticals or illicit drugs, and, if only for this reason, this list is not all-inclusive. Clinical evidence would suggest that marijuana use by patients on lithium can cause the lithium levels in the blood to increase, possibly to toxic levels (Ciraulo, Shader, Greenblatt, & Creelman, 2006). Given the fact that lithium has only a very narrow therapeutic window, and if too high may be fatal, the possible interaction between these compounds is potentially life-threatening. There is a single case report of a patient who used marijuana while taking the antidepressant medication fluoxetine who developed a possible drug-induced psychotic reaction; however, details are lacking about this case (Brust, 2004).

Individuals who use cocaine will often use marijuana in an attempt to counteract the agitation and excessive stimulation induced by high levels of cocaine use. It is known that marijuana use will cause an increase in the heart rate between 20 and 50%, and it is known that cocaine can cause a wide variety of cardiac problems (Hall & Degenhardt, 2005). Research is needed on the interactional effects of concurrent cocaine and marijuana use, either on previously healthy patients or on those with unsuspected or known cardiac disease.

Many individuals who use marijuana appear to be at increased risk for an AUD, and the simultaneous use of both compounds is common (Caulkins et al., 2015). This practice is potentially dangerous since marijuana inhibits nausea and vomiting. One of the body's natural defenses against poisons is to eject the poison from the body by vomiting. In theory, individuals who have ingested too much alcohol while using marijuana are at increased risk of a potentially fatal alcohol overdose since the body would be less able to eliminate the alcohol in the stomach that has yet to be absorbed (Caulkins et al., 2015; Craig, 2004).

As this rather short list demonstrates, there is a dire need for further research into potential interactional effects between marijuana and both pharmaceuticals as well as illicit drugs, especially given that most interactions that may be listed for prescriptions are theoretical in nature (Freeman & Murphy, 2016).

Methods of Marijuana Use

Although it is possible to inject THC into the body, this is a very difficult process. The preferred methods of marijuana use are oral ingestion (often called **edibles**) or by smoking (Brust, 2004; Erickson, 2007). Vaporization (often called **vaping**) has also become more common (Newmeyer, Swortwood, Abulseoud, & Huestis, 2017). Individuals who use oral routes used to be limited to baking marijuana into brownies or cookies; however, there are now a range of products such as chocolate laced with THC, a form of peanut brittle laced with THC, honey mixed with THC, and capsules that look like over-the-counter omega-3 fish oil capsules that contain THC rather than fish oils. In the past, when the THC content of marijuana was much lower, the preferred method of marijuana use was smoking. It is not known whether the strains of marijuana with higher levels of THC now being sold will make oral preparations more popular. However, early evidence suggests that in those states where marijuana sales have been legalized, the oral use of marijuana preparations has become more common. In these states, some forms of marijuana have been packaged to mimic popular candies and sweets (MacCoun & Mello, 2015). Further, some prepackaged oral preparations of marijuana appear to the casual observer to be a single serving, whereas the package contains more servings, leading to the potential for unintentional overdosing by inexperienced individuals (MacCoun & Mello, 2015).

Orally administered marijuana is absorbed slowly, the result being that the individual does not feel the first effects of THC until 30–120 minutes after ingesting it. A large amount of the THC ingested orally will be destroyed in the gastrointestinal tract by digestive juices, and only about 4–12% of the available THC will reach the individual's circulation (Drummer & Odell, 2001; Gold et al., 2004; Stimmel, 1997a). Thus, the individual using edibles must ingest approximately three times as much marijuana as someone smoking marijuana to achieve the same effect (Sadock et al., 2015). After oral ingestion, the peak THC levels are usually seen in 1–5 hours, and the effects last for 5 to possibly as long as 24 hours after ingestion (Brust, 2004; Drummer & Odell, 2001; Gruber & Pope, 2002). Oral ingestion does avoid the telltale smell of marijuana smoke, which would alert employers, law enforcement, or school officials that the individual has been using marijuana, but it makes it difficult if not impossible to titrate the individual's dose. This is more easily accomplished when marijuana is smoked, a practice that can be traced back for at least 5,000 years (Gruber & Pope, 2002; Walton, 2002). Neuropharmacologists disagree as to the amount of THC that reaches the circulation when marijuana is smoked.

Stephens and Roffman (2005) suggested that 30–80% of the available THC is destroyed in the process of smoking or lost in “side stream” smoke. Only 5–24% of the remaining THC was absorbed into the individual’s body (Stephens & Roffman, 2005). Other researchers have suggested that almost 60% of the available THC was absorbed into the body when it was smoked (Gold et al., 2004; Lehne, 2013). These two estimates of the amount of THC absorbed into the individual’s body might reflect the fact that there is significant intraindividual variability in THC absorption rates when it is smoked. However, as these discrepant estimates suggest, there is much to be learned about the process of marijuana smoking, and the absorption of THC when it is smoked.

Although it might be intermixed with other compounds, marijuana is usually smoked alone in cigarettes commonly called *joints*. The average marijuana joint contains about 0.25 grams of marijuana, providing approximately 7 mg of THC (Kögel et al., 2017). Certainly, this can vary greatly, based on the joint as well as the potency of the marijuana. A variation on the marijuana cigarette is the *blunt*, made by removing some of the outer leaves of a cigar, unrolling it, filling the core with high-potency marijuana mixed with chopped cigar tobacco, then re-rolling the cigar (Gruber & Pope, 2002). When it is smoked in this manner, individuals often report some degree of stimulation, possibly from the nicotine in the tobacco in addition to marijuana’s sedating effects.

The process of smoking a joint is somewhat different from that used to smoke normal tobacco cigarettes. The individual must inhale the smoke deeply into his/her lungs, then hold his/her breath for as long as possible (ideally 20–30 seconds) in an attempt to allow as much THC as possible to cross over from the lungs into the general circulation. The effects of the THC that does enter the circulation are felt within seconds to perhaps a few minutes (Brust, 2004). When smoked, the effects of marijuana reach peak intensity in 20–30 minutes, and begin to decline in about an hour (McDowell, 2005; Sadock et al., 2015). THC is relatively potent, and the individual must inhale only 25–50 micrograms of THC for every kilogram of body weight, while the oral user must ingest 50–200 micrograms of THC per kilogram of body weight, to achieve a marijuana high (Mann, 2000). Exceptionally high blood levels of THC have been reported to have a hallucinatory effect (Lezak, Howieson, Bingler, & Tranel, 2012), although Mann (2000) suggested that this would require a dose five times higher than those usually used in the United States. Thus, hallucinations are only rarely reported in the United States in spite of marijuana’s official classification as a hallucinogenic compound.

Subjective Effects of Marijuana Use

Those who smoke marijuana achieve the strongest effects, producing a mild sense of euphoria, relaxation, and some sensory distortions that alter the individual’s perception of ordinary activities such as eating, watching television or movies, and having sex (Hall & Degenhardt, 2005). Some individuals smoking marijuana report enhanced perception of sounds and colors as well (Earlywine, 2005; Zevin & Benowitz, 2007). In social settings, those who smoke marijuana are prone to infectious laughter, excessive talkativeness, and a feeling of relaxation. Individuals who smoke high-potency marijuana report a **synesthesia**¹⁶-like experience, in which the sensations of one sensory modality slip over into another (Earlywine, 2006). Over half of individuals who use marijuana report enhanced tactile sensations, and while the sense of taste is not improved, they may speak of enjoying taste sensations more (Earlywine, 2006). Some individuals also report that marijuana’s effects contribute to enhanced sexual pleasure (Earlywine, 2006). These claims have not been verified by scientific research, and, as will be discussed later in this chapter, men may be impacted by a host of marijuana-related sexual dysfunctions that appear to negate its potential to enhance sexual pleasure.

The effects of marijuana progress through two phases, which are influenced, in part, by the individual’s expectations (Brust, 2004). In the first phase, which begins shortly after THC enters the circulation, the individual experiences some mild anxiety and decreased salivation. This phase is thought to last from 2 to 4 hours (Grinspoon et al., 2005; O’Brien, 2006; Sadock et al., 2015; Zevin & Benowitz, 2007). The selective activation of the amygdala and cingulate cortex regions of the brain by THC, combined with the unexpected increase in cardiac rate and marijuana-induced periods of depersonalization, may be reasons why many inexperienced in marijuana use experience some degree of anxiety after smoking marijuana.

However, most of those experienced in using marijuana report a positive experience from marijuana use, including mild euphoria, a sense of relaxation, and a reduction in subjective anxiety levels (Grinspoon et al., 2005; Hall & Degenhardt, 2005; O’Brien, 2011). These effects of marijuana appear to be caused by the THC isomer cannabidiol CBD, which appears to selectively suppress the function of those regions of the brain involved in the fear response¹⁷ (Fusar-Poli et al., 2009). These effects blend into the second phase of marijuana intoxication, in which the individual will experience

¹⁶See Glossary.

¹⁷In this case.

residual psychomotor problems, mood swings, and possible depression (Schatman, 2015). These feelings last for at least 5 to 12 hours after a single dose, suggesting that marijuana's effects on the individual should be classified as falling into either the period of acute or extended effects (Freimuth, 2005; O'Brien, 2006; Sadock et al., 2015; Tomb, 2008).

Clinicians often hear patients who struggle with depression claim that they use marijuana because it helps their depression. Research has demonstrated that very low doses of marijuana do seem to stimulate the release of serotonin in the brain, and thus might have an antidepressant effect in much the same manner as the selective serotonin reuptake inhibitors (SSRIs). However, there is only a very narrow dosing window for this effect, and if the individual should use more marijuana than necessary, it can contribute to the feelings of depression (Bambico, Katz, Debonnel, & Govvi, 2007; Washron & Zweben, 2006). Thus, marijuana's antidepressant effects are too limited to be of clinical significance.

Those who misuse marijuana often report a sense of being on the threshold of a significant personal insight, but that they are unable to put this insight into words. Such drug-induced insights are rarely recalled after the period of acute intoxication ends. Further, marijuana-related creative efforts are usually found to be somewhat less than inspirational when the individual recovers from the period of acute intoxication. In such cases, the individual's subjective sense of insight and creativity appears to reflect the drug's effects on the brain rather than any actual new perception of the self or the world around the individual.

Adverse Effects of Marijuana Misuse

Dangers of Marijuana Misuse: An Ongoing Debate

Marijuana was and continues to be viewed by many people as being relatively harmless. The effective dose is estimated to be between 1/20,000th and 1/40,000th the lethal dose (Grinspoon et al., 2005). To express this safety margin in other terms, it has been estimated that a 160-pound person would have to smoke 900 marijuana cigarettes simultaneously to reach the lethal level (Cloud, 2002). An even higher estimate was offered by Schlosser (2003), who suggested that the average person would need to smoke 100 *pounds* of marijuana every minute for 15 minutes to achieve a lethal overdose.¹⁸ In contrast to the estimated 200,000 deaths

caused by the other forms of illicit drug use around the world each year, there are only two documented cases of a lethal marijuana overdose, although Coghlan (2009) did not provide specific information about these alleged marijuana overdose deaths. While this information would suggest that marijuana has an impressive safety margin, it is not totally without risk.

Known and Suspected Adverse Effects of Marijuana Misuse

In the last decades of the 20th century, scientists began to identify adverse effects of marijuana use (Aharonovich et al., 2005). However, with well over 400 known compounds and more than 2,000 known metabolites of these compounds being produced during the biotransformation process, there is much to be discovered about marijuana's short-term and long-term adverse effects. Some of these metabolites might remain in the individual's body for weeks after a single period of marijuana use. In spite of this, research into the physical effects of marijuana on the brain has been "surprisingly scarce" (Aharonovich et al., 2005, p. 1057).

There have been rare reports of **anaphylactic**¹⁹ reactions in individuals who misuse marijuana, although it is not clear whether these reactions were triggered by the marijuana itself, or by contaminants or adulterants found in illicit marijuana samples (Brust, 2004). It is not uncommon for illicit marijuana to be adulterated, and these compounds add to the flood of chemicals introduced into the body when an individual uses marijuana. To further cloud the issue, illicit marijuana is often exposed to herbicides sprayed on it by law enforcement officials in an attempt to destroy the plants before they are harvested and sold. If the plants are nevertheless harvested and sold, those herbicides are still on the plant, and will also be introduced into the body.

A more common reaction for those who only occasionally use marijuana is the development of "bloodshot" eyes (Mendelson & Mello, 2008; Mendelson, Mello, Schuckit, & Segal, 2006). This effect is relatively harmless, and is caused by marijuana-induced dilation of the blood vessels in the conjunctiva of the eyes. It can be quite striking to see for the first time. However, 40–60% of individuals will report at least one other adverse effect beyond bloodshot eyes (Hubbard et al., 1999). Further, marijuana intoxication impairs the motor skills necessary to safely drive a motor vehicle on about the same level as does a blood alcohol level of between 0.07 and 0.1% (Hall & Degenhardt, 2005), possibly in part due to its ability to interfere with normal

¹⁸It should be noted that some individuals have made commendable efforts to reach this level of marijuana intoxication, although apparently with little success.

¹⁹See Glossary.

depth perception. These impacts include not only motor skills, but reaction time, memory, attention, and decision-making skills (Capler, Bilsker, Van Pelt, & MacPherson, 2017). Even occasional episodes of marijuana use increase the individual's risk of being in a motor vehicle accident by 300–700%, again possibly because of marijuana-induced loss of depth perception (Brust, 2004; Lamon et al., 2005).

Marijuana can induce a splitting of consciousness or even periods of depersonalization (Earlywine, 2005; Johns, 2001; Schatman, 2015). While low blood levels of THC appear to be anxiolytic, higher blood THC levels, such as those easily achieved with the more potent forms of marijuana being sold today, appear to be more likely to induce anxiety (Schatman, 2015). This might be one reason why 50–60% of individuals who use marijuana report experiencing at least one episode of marijuana-induced anxiety (O'Brien, 2006). Since individuals who smoke marijuana are able to titrate their dose more easily than those who ingest it orally, there is a tendency for those who use oral forms to experience anxiety more than those who smoke marijuana, since the latter group can simply stop smoking it if they find its effects uncomfortable (Brust, 2004; Gold et al., 2004). Usually, the only treatment that is necessary is a gentle reassurance that it will soon pass (Brust, 2004; Sadock et al., 2015).

Marijuana use has been identified as a cause of increased heart rate and arrhythmias. There have also been rare reports of myocardial infarction and atrial fibrillation in persons who have just used marijuana, although the causal mechanism still remains to be identified (Khan, Morrow, & McCarron, 2009; Schatman, 2015). There are reports of individuals using marijuana experiencing **angina**,²⁰ especially if they have preexisting coronary insufficiency, and persons with known or suspected cardiac problems are advised not to use marijuana (Mendelson & Mello, 2010; Mendelson et al., 2006). Further, the particulates generated by smoking marijuana cause a dose-related reduction in pulmonary function. Unlike tobacco smoking, which produces microscopic particles that block the lung passages in the lowest levels of the lungs, marijuana smoking produces larger particles that block the larger air passages of the respiratory system (Aldington et al., 2007; Schatman, 2015).

There is one case report of a child suffering an episode of transient global amnesia after the child was accidentally exposed to marijuana, which resolved after a period of several hours (Prem & Uzoma, 2004). Although often believed to be an aphrodisiac, even limited marijuana use is known to reduce sexual desire, and for males who use marijuana it

may result in erectile dysfunction, reduced sperm count, and delayed ejaculation (Greydanus & Patel, 2005; Hall & Degenhardt, 2005).

PSYCHOTIC REACTIONS

Researchers have long been aware that individuals who use marijuana are at increased risk for psychotic reactions (Large & Nielssen, 2017; Schatman, 2015; Welch, 2009). Most marijuana-induced psychotic reactions are short-lived, clearing up in a few hours or days (Johns, 2001). There is debate over whether an ongoing psychosis reflected a predisposition toward a psychosis that was possibly unmasked by marijuana use (Compton et al., 2009; Hall & Degenhardt, 2005), or was induced by the individual's marijuana use. The latter theory is supported by the findings of McGrath and colleagues (2010), who found an increased risk of psychosis in young adulthood for individuals who engaged in marijuana use earlier in life as compared to siblings who did not use marijuana.

If this theory is true, then what initially presented as a marijuana-related psychotic reaction might activate the potential psychosis within the individual and it may potentially become permanent. This is supported by the research of Helle and colleagues (2016). The age at which the individual begins to use marijuana is one apparent critical variable in the development of a later psychotic reaction (Large & Nielssen, 2017). Research evidence suggests that individuals who had used marijuana during adolescence, especially before the age of 15, have a higher incidence of schizophrenia later in life (Lezak et al., 2012; Raby, 2009). Another critical variable affecting the potential emergence of a marijuana-related psychosis is the intensity of use. Those individuals who smoke marijuana more often appear to have a higher risk of developing schizophrenia, possibly 3 years earlier than those who do not use (Helle et al., 2016). Another study conducted in Sweden revealed that army recruits who had used marijuana more than 50 times had a 670% higher incidence of becoming psychotic later in life than those who had not used (Iverson, 2005).

There is preliminary evidence suggesting that the body's endocannabinoids can produce transient schizophrenia-like symptoms. Since THC binds at the cannabinoid receptor site 40 times as strongly as do the natural endocannabinoids, this theory might account for the apparent relationship between marijuana use and an increased incidence of schizophrenia. This theory is supported by the fact that the regions of the brain known as the striatum and the cingulate both have a high number of cannabinoid receptor sites (Bhattacharyya et al., 2009) and are thought to be involved in the development of the symptoms of schizophrenia. An alternative theory is that marijuana can interfere with the normal function of the endocannabinoid 2-arachidonoylglycerol in the cortex and hippocampus of the brain, with

²⁰See Glossary.

the same result. Yet a third hypothetical explanation for the apparent relationship between marijuana use and the development of psychosis was offered by Feilding and Morrison (2010). The authors, drawing upon recent research into the role of the compound cannabidiol CBD, noted that as strains of marijuana have been developed with higher levels of THC, CBD levels have dropped almost proportionally. Recent evidence suggests that CBD has an antipsychotic effect, theoretically counteracting the potential for THC to induce a psychosis. In essence, by developing new strains of marijuana with higher levels of THC, an unintended side effect has been that the more potent strains of marijuana have lower levels of CBD, a compound that might protect the user from psychosis. As these three competing theories suggest, there is still a great deal to be discovered about the effects of the various chemicals found in marijuana on the brain.

METABOLIC EFFECTS

In the brain, the endocannabinoids are known to be involved in many different body regulatory functions, including energy metabolism and appetite regulation. For this reason, Muniyappa and colleagues (2013) attempted to determine the impact of marijuana use on the body's metabolism. Surprisingly, although marijuana use did cause some transient metabolic changes, the authors found little if any evidence suggesting long-term metabolic system changes in those who smoke marijuana chronically.

NEUROLOGICAL CHANGES

Using new high-resolution structural magnetic resonance imaging (MRI) technology, Yucel and colleagues (2008) found that individuals who smoke marijuana chronically had an approximate 12% reduction in volume of the hippocampus and a 6% reduction in the size of the amygdala region of the brain. These regions of the brain have a high density of cannabinoid receptors, and there was a clear relationship between duration of marijuana use and the degree of shrinkage in these regions of the brain, although it is not clear at this time whether this reduction in regional brain volume is permanent. It also is not known whether the observed changes in regional brain size contributes to the report that persons who have used a hallucinogenic such as LSD often experience marijuana-triggered "flashbacks" (Hall & Degenhardt, 2005; Sadock et al., 2015). Such flashbacks are usually limited to the six-month period following the individual's last use of marijuana, and usually will stop on their own.

A small but growing body of evidence suggests that chronic marijuana misuse can cause cognitive deficits in the brain (Khamisi, 2013; Mizrahi, Watts, & Tseng, 2017; Schatman, 2015; Vik, Cellucci, Jarchow, & Hedt, 2004; Wattereus, Badcock, Di Prinzio, Martin-Iverson, & Morgan, 2017). These cognitive deficits are often detectable on

neuropsychological tests for up to 7–14 days after those who habitually use marijuana last used (Pope et al., 2001; Vik et al., 2004). Memory deficits appear to be progressively worse in those who use heavily who started to smoke marijuana heavily in their teen years (Meier et al., 2012). Neuropsychological testing carried out when teens who smoked marijuana had reached their mid-thirties suggested that the effects of adolescent marijuana use might alter the cognitive development of the individual for longer periods of time than once was thought true (Schatman, 2015). Long-term marijuana use may cause neurocognitive impairment for up to 2 years after last use of marijuana, and measured IQ is approximately 8 points lower than that of those who do not use (Gonzalez et al., 2009; Khamisi, 2013; Khan et al., 2009).

Many individuals who use marijuana on a chronic basis have abnormal patterns of electrical activity on electroencephalograph (EEG) studies. It is possible that these EEG changes predate the individual's marijuana or other chemical abuse, although there is little evidence to support this hypothesis. Repeated, heavy episodes of marijuana use are associated with dose-dependent changes in the brain's internal electrical activity (Herning, Better, & Cadet, 2008). The authors speculated that the observed EEG changes might reflect altered brain perfusion (blood flow in the brain). Sneider et al. (2006) suggested that the changes in regional blood flow patterns in the individual's brain might persist for at least the first few weeks after the individual stopped using marijuana.

Under normal conditions, the occasional activation of the endogenous cannabinoid CB1 receptor might have a neuroprotective effect (Freedman, 2008). However, the persistent activation of this receptor site appears to make the CB1 receptor less responsive, thus negating this neuroprotective function. The affected neurons are no longer protected against the increased levels of excitation and neural death produced by such conditions as schizophrenia or continual marijuana use. This might account for the findings of the research team of Matochik, Eldreth, Cadet, and Bolla (2005), who found evidence of significant levels of neural tissue loss in the right para-hippocampal gyrus and in the left parietal lobe in the brains of 11 individuals on neuroimaging studies. This loss of neural tissue was strongly correlated with the duration of marijuana use, according to the authors. Paradoxically, Jacobus and colleagues (2009) found evidence that adolescents who use marijuana appear to have less damage to the "**white matter**"²¹ of the brain after episodes of binge drinking, as compared with adolescents who engage in binge drinking but who do not smoke marijuana. The mechanism

²¹See Glossary.

by which marijuana might provide a neuroprotective effect in such circumstances is not known at this time, and the findings of this study must be replicated in future research to confirm that this process does indeed take place.

EFFECTS OF HABITUAL MARIJUANA USE ON SLEEP

The habitual use of marijuana suppresses REM sleep, although it is not clear whether isolated episodes of marijuana use have any significant impact on REM sleep (McDowell, 2005). The consequences of REM sleep suppression on the individual's health have yet to be determined, although some research has suggested that long-term REM sleep suppression might negatively affect the individual's health. Ultimately, further research is needed, but at this time it seems that THC in particular may negatively impact the ability to get quality sleep on a long-term basis (Babson, Sottile, & Morabito, 2017).

ON THE PULMONARY SYSTEM

Individuals who use marijuana tend to smoke fewer joints than those who use tobacco smoke cigarettes, but the joints are unfiltered, increasing the user's exposure to microscopic contaminants in marijuana. This does not appear to result in damage to the pulmonary system in those who only rarely smoke marijuana (Pletcher et al., 2012). However, researchers have found precancerous changes in the cells of the respiratory tract in those who use marijuana chronically, similar to those seen in those who smoke tobacco (Gold et al., 2004; Tashkin, 2005; Tetrault et al., 2007). Preliminary evidence would suggest that smoking one marijuana joint a day might increase the individual's risk for lung cancer as much as if s/he were to smoke a pack of cigarettes a day (Brambilla & Colonna, 2008). The authors went on to state that marijuana smokers who had smoked just one joint a day for 10 years had a 570% higher risk of lung cancer than those who did not smoke marijuana. However, since 70% of those who smoke marijuana also smoke cigarettes (Filbey, McQueeney, Kadamangudi, Bice, & Ketcherside, 2015), it is difficult to isolate the effects of smoked marijuana from the combined effects of smoked marijuana and tobacco. In their preliminary study, Filbey et al. (2015) found that individuals who smoked marijuana demonstrated measurable memory deficits, but that those who smoked marijuana and who also smoked tobacco products appeared to have less memory loss than those who smoked marijuana alone. However, this improvement in memory function is overshadowed by the potential for physical damage inherent in the use of marijuana, tobacco, or a mixture of these compounds.

Individuals who smoke marijuana were also found to have an increased incidence of coughing and wheezing, in a manner similar to that seen in those who smoke cigarettes (Khan et al., 2009; Tetrault et al., 2007). Marijuana use by

individuals who also smoke cigarettes appears to increase the individual's risk for the development of chronic obstructive pulmonary disease (COPD) later in life (Macleod et al., 2015; Tan et al., 2009). This is perhaps understandable: Those who smoke marijuana are exposed to virtually all the toxic compounds found in tobacco cigarettes except nicotine. If they were to smoke a blunt, the individual would be exposed to *all* of the toxins found in tobacco, plus other toxins found in the marijuana (Gruber & Pope, 2002). The typical marijuana cigarette has 10–20 times as much “tar” as tobacco cigarettes (Nelson, 2000). Those who smoke marijuana are also exposed to higher levels of carbon monoxide than those who smoke tobacco, although the exact significance of this finding is not clear since most individuals who smoke marijuana also smoke cigarettes.

IMMUNOSUPPRESSANT EFFECTS

Animal research confirms that heavy marijuana use appears to suppress the immune system's effectiveness (Abrams et al., 2003; Gold et al., 2004). This finding is of potential significance for those persons who struggle with viral infections such as the hepatitis viruses or HIV,²² since it might interfere with the body's ability to fight off the invading organism.

MARIJUANA AS A POSSIBLE CAUSAL AGENT FOR THE DEVELOPMENT OF CANCER

It has long been known that marijuana smoking reduces the effectiveness of the respiratory system in resisting infection (Gruber & Pope, 2002; Hall & Degenhardt, 2005). It has been hypothesized that the body's “scavenger” cells are on constant patrol for cells that are genetically different from those of the body, which would include external pathogens and cells in the body whose genetic structure has been disrupted. This is understandable since marijuana smoke has been found to contain many of the same carcinogens found in tobacco cigarettes, often in higher amounts than in regular tobacco cigarettes. Marijuana-induced suppression of the body's natural defenses combined with the exposure to these carcinogenic compounds might explain why those who smoke marijuana are at increased risk for cancer of the mouth, tongue, throat, and lungs (Gruber & Pope, 2002; Hall & Degenhardt, 2005; Han, Gfoerer, & Colliver, 2010).

There is also an emerging body of evidence suggesting that marijuana use increases the male's risk for cancer of the testicles, especially the more aggressive nonseminomas form of testicular cancer (Daling et al., 2009; Lacson et al., 2012). Lacson and colleagues (2012) found that the risk of cancer of the testicles increased by almost 100% if the individual had ever engaged in marijuana use, while

²²Discussed in Chapter 36.

Daling and colleagues (2009) suggested on the basis of their research that the risk of marijuana-associated testicular cancer was influenced by factors such as the duration of use, frequency of use, and the time when the individual first began to use marijuana. These findings appear to justify the decision by the state of California to require medical marijuana dispensaries to label marijuana as a potential carcinogen (Dembosky, 2009).

REPRODUCTION SYSTEM DYSFUNCTIONS

Chronic marijuana use has been implicated as the cause of a number of reproductive system dysfunctions such as reduced sperm count, lower testosterone levels, and smaller testicular size in males who use marijuana (Hubbard et al., 1999; Schuckit, 2006a). Habitual use of marijuana in females has been shown to be related to menstrual abnormalities, including possible failure to ovulate (Gold et al., 2004; Hubbard et al., 1999). These problems are so severe that women who wish to conceive are advised to abstain from marijuana use prior to attempting to become pregnant.

THE CIRCULATORY SYSTEM

Heavy marijuana use has been identified as a cause of cardiac arrhythmias, although the individual who uses heavily can develop some tolerance to this effect (Khan et al., 2009). Older individuals who smoked marijuana and who suffered an acute myocardial infarction (heart attack) were less likely to survive than were nonsmokers of the same age who had suffered a similar cardiac event (Mukamal, Maclure, Muller, & Mittleman, 2008). The authors also found that heart attack survivors who continued to use marijuana were at higher risk for death than were those who did not smoke marijuana and who survived. It was not clear whether these findings were a direct result of the individual's marijuana use or whether there were other causes (e.g., cigarette smoking) that contributed to the findings of this study.

Marijuana use, for example, is associated with a 30–50% increase in cardiac rate that might last for as long as 3 hours after the initiation of an episode of marijuana use (Craig, 2004; Hall & Degenhardt, 2005). This is potentially harmful for individuals who have a cardiac condition. Marijuana use is also associated with a reduction in the strength of cardiac muscle contractions and the amount of oxygen reaching cardiac tissues, which again are conclusions of importance to patients with cardiac disease. This also might be one mechanism by which marijuana use causes an increased risk of heart attacks in older individuals during the first few hours following the initiation of an episode of use (“Marijuana-related deaths?,” 2002; Mittleman, Lewis, Maclure, Sherwood, & Muller, 2001; Mukamal et al., 2008; Schuckit, 2006a).

OTHER CONDITIONS ASSOCIATED WITH MARIJUANA MISUSE

There is an emerging body of evidence that suggests that long-term marijuana use might contribute to periodontal disease (Thomson et al., 2008). The authors reported that after examinations of 903 young adults, that they found evidence of periodontal disease in 32% of those who used marijuana at least once a week, 12% of those who used marijuana less frequently than once a week, and only 4% of those who did not use in their research sample. This was independent of each individual's tobacco use, which itself increased the individual's risk for potential periodontal disease by a small margin, the authors suggested.

A more disturbing finding is that marijuana use seems to be associated with a more rapid progression of liver damage in patients infected with the hepatitis C virus²³ (Ishida et al., 2008). The authors speculated that at least some of the individuals identified in their research sample had switched from alcohol to marijuana because of their fear that their alcohol use might accelerate the damage being done to their liver by the viral infection. However, marijuana use might also be associated with an acceleration in liver damage in hepatitis C patients, the authors observed.

THE “AMOTIVATIONAL SYNDROME”

Scientists have found conflicting evidence that chronic marijuana use might cause the so-called “amotivational” syndrome. This hypothetical condition is marked by short attention span, decreased drive and ambition, easy distractibility, and a tendency not to make plans beyond the present day (Hall & Degenhardt, 2005). Indirect evidence that such a condition might exist was provided by Gruber, Pope, Hudson, and Yurgelun-Todd (2003). The authors compared the psychological and demographic measures of 108 individuals who had smoked marijuana more than 5,000 times against 72 age-matched control subjects who reported having abused marijuana 50 times or less. The authors found that those individuals with the greatest level of marijuana use had significantly lower income and educational achievement levels than did the control group. While suggestive, this study does not answer the question of whether these findings reflect the effects of marijuana, or if individuals prone to heavy marijuana use tend to have less drive and initiative prior to their marijuana use.

Many researchers have challenged the very existence of the amotivational syndrome, in part because even those who use marijuana heavily demonstrate remarkable energy in the pursuit of their (marijuana-centered) goals. It has been

²³Discussed in Chapter 36.

suggested that the amotivational syndrome reflects nothing more than the acute effects of marijuana intoxication on the individual (Johns, 2001) or the person's personality style rather than a drug-induced effect (Sadock et al., 2015). Thus, the question of whether there is a specific amotivational syndrome that might be attributed to marijuana use has not been determined as of this time (Brunton, Parker, Blumenthal, & Buxton, 2008).

Marijuana-Induced Violence

In the 1930s and 1940s, it was widely believed that marijuana use would trigger episodes of violence. This belief was reinforced by politicians who wished to further their political agenda by using it as a justification to outlaw marijuana. However, researchers during that era failed to find evidence to support the theory that marijuana use could trigger episodes of violence. Indeed, even in past decades, "only the unsophisticated continue to believe that cannabis [abuse] leads to violence and crime" (Grinspoon et al., 2005, p. 267). Clinicians believed that the sedating and euphoric effects of marijuana would *reduce* the tendency toward violent behavior (Grinspoon et al., 2005; Husak, 2004).

However, it was theorized that the individual who used on a chronic basis would be more tolerant to the sedating effects of marijuana, and thus capable of reacting violently if they have a predisposition toward violence (Walton, 2002). Ansell, Laws, Roche, and Sinha (2015) recently noted that research into the adverse effects of marijuana were based on research carried out in controlled laboratory settings. How marijuana use affects the individual outside of the laboratory has not been well studied. Ansell and colleagues (2015) used modern telecommunications devices to contact research participants each day, and found that their participants reported an increase in hostile behavior, and increased perception of hostility in others, on the days when they used marijuana. Given the increasing acceptance of social marijuana use, the authors called for further research into this topic.

Addiction to Marijuana²⁴

Contrary to the belief of many people, marijuana is addictive, although there is some degree of controversy about the danger of marijuana addiction. It has been estimated that between 8 and 20% of long-term marijuana abusers will become dependent on it (Budney, Roffman, Stephens, & Walker, 2007; Volkow, Frieden, Hyde, & Cha, 2014; Zevin & Benowitz, 2007). The risk of marijuana dependence might be increased

if the individual is using a form of marijuana that has been bred to have a high THC content (Khamisi, 2013). There is limited data about marijuana addiction, although addiction to it appears to be associated with a loss of economic and social status (Cerde et al., 2016), and further research into this phenomenon is necessary. Others indicate that it is just as addictive and dangerous as other drugs that are misused, with significant harms related to misuse of marijuana (Miller, Oberbarnscheidt, & Gold, 2017). Recent evidence does point toward marijuana use impacting the brain in a way that may make the individual more likely to use other drugs and develop other addictions (Martz et al., 2016).

Marijuana Withdrawal Syndrome

Marijuana does not induce the same dramatic withdrawal symptoms seen in those dependent on alcohol- or narcotics who discontinue the misuse of their desired drug(s). For this reason, people have long underestimated the addiction potential of marijuana. However, tolerance, one of the hallmarks of physical addiction to a substance, does rapidly develop to marijuana (Stephens & Roffman, 2005; Welch, 2009). Approximately one-half of persons in treatment for cannabis use disorder report experiencing some withdrawal symptoms upon cessation of marijuana use.

There is a well-documented cannabis withdrawal syndrome that can include irritability, anger, aggression, anxiety, depression, insomnia, unusual dreams, restlessness, sweating, nausea, tachycardia, decreased appetite, weight loss, a craving for marijuana, and vomiting (Brunton et al., 2008; Budney et al., 2007; Danovitch & Gorelick, 2012; Kelly & Leamon, Wright & Myrick, 2008; Levin, 2015; Raby, 2009; Schatman, 2015; Welch, 2009). These withdrawal symptoms begin 1–3 days after the individual's last use of marijuana, peak between the second and tenth days, and the total duration of the marijuana withdrawal syndrome has been estimated to last between 12 and 115 days, depending on the duration and intensity with which the individual was using marijuana (Budney, Moore, Bandrey, & Hughes, 2003; Leamon et al., 2008; Sussman & Westreich, 2003). This withdrawal syndrome is flu-like in intensity, although in some individuals it might approach the intensity of nicotine withdrawal (Budney et al., 2007; Vandry, Budney, & Ligouori, 2008). There is no specific treatment for marijuana withdrawal other than complete abstinence from all drugs (Danovitch & Gorelick, 2012). However, the marijuana withdrawal syndrome can serve as a "trigger" for further marijuana use, starting the individual back down the road toward marijuana addiction (Crowley, 2007). As this evidence suggests, marijuana does meet the established criteria for an addictive compound.

²⁴Unfortunately, it is not possible to determine *who* will become addicted to marijuana, and so its use is not recommended if only for this reason.

Marijuana Use and the *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition²⁵

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013) identified five subforms of the marijuana-related disorders:

- *Cannabis intoxication*
- *Cannabis use disorder*
- *Cannabis withdrawal*
- *Other cannabis-induced disorders*
- *Unspecified cannabis-related disorder*

For unknown reasons, the authors of the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013) elected not to use the term *marijuana dependence* but instead used the more ambiguous term *cannabis use disorder*. The diagnostic criteria for cannabis-dependence are outlined in *DSM-5* but essentially are unchanged from the 4th edition of the *Diagnostic and Statistical Manual*. The only known “biological marker” for cannabis use is the detection of marijuana metabolites in the person’s blood or urine according to the American Psychiatric Association (2013). The *DSM-5* does acknowledge that the nonproblematic use of cannabis is possible, and notes that the differentiation between nonproblematic use and problematic use often is complicated by denial or polydrug abuse. Some of the associated life problems associated with the use of marijuana include (but are not limited to): anxiety, a drug-induced persistent depression, a delusional disorder, and a lack of motivation according to the *DSM-5*.

The diagnostic signs of cannabis intoxication are essentially the same as those outlined in this chapter, although the *DSM-5* accepts the possibility that the individual might experience what it terms “perceptual disturbances” (p. 516), which is to say hallucinations. The signs of marijuana withdrawal identified by the *DSM-5* are essentially the same as those outlined in this chapter, and are thought to develop 24–72 hours after the person’s last marijuana use. As was discussed in this chapter, marijuana use is associated with the development of various conditions such as a sleep cycle disturbance or delirium, which fall under the rubric of

Other Cannabis Induced Disorders in the *DSM-5*. The classification of *Unspecified Cannabis-Related Disorders* identifies those individuals whose marijuana use has resulted in significant impairment in their social, occupational, or social spheres of their lives but whose marijuana use does not fully meet the identified criteria for marijuana a marijuana use disorder.

Chapter Summary

Cannabis has been cultivated for its fiber for thousands of years, and at one point no less a person than George Washington cultivated it as a commercial crop for hemp fiber, which has been used for a variety of purposes over the course of history. However, at some unknown point it was discovered that some varieties of cannabis produced a substance, later to be called THC, that produced a sense of euphoria if smoked. Cannabis was thus transformed from a useful plant into a substance to misuse. The misuse of marijuana smoldered through the 1930s and 1940s, emerging as a substance to misuse for certain segments of the population in the 1950s. During the 1960s, it emerged as a popular illicit drug in the United States, and a large demand for it developed. Suppliers sought to develop strains of marijuana with ever-increasing levels of THC for its enhanced effects, to claim a larger share of the marijuana market during a time when its use became a mark of rebellion against the established authorities. These forces interacted to make its use so common that by the start of the 21st century more than 50% of adults in the United States were thought to have used it at least once.

In spite of evidence to the contrary, the federal government continues to maintain that there is no medicinal value in any compound found in marijuana. Its classification by the DEA as a Schedule I substance has made objective research into potential medical applications of marijuana almost impossible (Gerich et al., 2015). In spite of this circular reasoning, physicians have started to accept the possibility that there are indeed possible benefits of marijuana use for some patients with certain conditions, and “medical” marijuana is now legal in many states, although technically federal law overrides state law. Proponents of the lifting of marijuana-use restrictions point to its relative safety; however, there is an emerging body of evidence suggesting that the chronic use of marijuana for recreational purposes is not without certain dangers. Further, it has been found to be an addictive substance, capable of producing a characteristic withdrawal syndrome. This information is certain to become part of the controversy surrounding the use, and possible misuse, of marijuana in the 21st century.

²⁵The material presented here is to illustrate the relationship between the marijuana use disorders and the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition. This material should not be interpreted as, nor should it be used as, a diagnostic manual.

Opioid Use and Misuse

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 11.1** Understand the history of natural and synthetic opioids
- 11.2** Understand the medical uses of opioids
- 11.3** Comprehend the complications of opioid use when used medically
- 11.4** Describe the consequences of opioid misuse
- 11.5** Comprehend the scope of the problem of opioid misuse
- 11.6** Understand the complications caused by misuse of opioids
- 11.7** Understand the *DSM* criteria for opioid-related disorders

Introduction

The experience of pain is something of an enigma to modern science: It is the oldest problem known to medicine, and yet there is no objective way to measure the intensity of pain (Chapman & Okifuji, 2004; Johannes, Le, Zhou, Johnston, & Dworkin, 2010). Pain can be experienced as either an acute or chronic condition (Meldrum, 2003). Each year in the United States alone more than 70% of adults will experience at least one episode of acute pain, and approximately 30% of adults will experience a period of chronic pain (defined as lasting 6 months or longer) (Johannes et al., 2010; Meldrum, 2003; Williams, 2004). However, in spite of much research, the experience and treatment of pain remains elusive. Throughout much of history, treatment was virtually synonymous with the use of opium; however, with the advent of the chemical revolution in the late 19th century, morphine and codeine were isolated from opium. In the time since then, pharmaceutical companies have churned out a plethora of new synthetic or semisynthetic variations of these two compounds. Because of their ability to induce sleep these compounds are classified as *narcotics*, or *narcotic analgesics*.

As a class, the narcotic analgesics have an addictive potential that is not well understood by clinicians. However, because of this potential for misuse, both physicians and the general public tend to view these medications with distrust in spite of their potential to relieve moderate to severe levels of acute pain. Unfortunately, the legal definition of “narcotic” is different from the pharmacological definition. Legally, cocaine is classified as a “narcotic” but does not have a chemical

structure similar to the opioids. In this chapter, the term “narcotic” or “opiate” will be used for compounds that produce effects similar to those of morphine or which are derived from opium. Opioid is a broader term, encompassing all substances that bind to opioid receptors in the body, which would include synthetic substances as well as endogenous substances (Reed, Picetti, Butelman, & Kreek, 2015). Myths about narcotic analgesics have been repeated so often that many have been incorporated into professional journals and textbooks as clinical “fact,” further complicating pain control (Vourakis, 1998). For example, many physicians *under-prescribe* narcotic analgesics to persons in pain and then view the request for additional analgesics by the patient as evidence of drug-seeking behavior, as opposed to a person who simply has not received an adequate dose for analgesia (Carvey, 1998; Kuhl, 2002). It has been estimated that as many as 73% of persons in moderate to severe levels of pain receive less than adequate doses of narcotic analgesics because of the physician’s fear of an **iatrogenic**¹ substance use disorder (SUD) (Gunderson & Stimmel, 2004; Stimmel, 1997a).

Each year in the United States, more than 3% of the general population receives a prescription for a narcotic analgesic for long-term pain control (Califf, Woodcock, & Ostroff, 2016; Dunn et al., 2010). Narcotic analgesics are increasingly being used to treat chronic pain as well, although this practice is still controversial and has been challenged by some researchers as being unwarranted in long-term pain control (Alford, 2016; Chou et al., 2015).

Regardless of why they are prescribed, some of these medications are diverted to the illicit drug market, while other narcotic analgesics are misused by the person for whom they were prescribed. In 2010,² there were 16,500 known deaths from prescribed narcotic analgesics which were misused in some way (Dajer, 2015). An excellent example of prescription narcotic misuse is provided by the pharmaceutical OxyContin®, which was introduced to control moderate to severe levels of pain, only to emerge as a significant part of the drug problem in the United States (Meier, 2003).³ There was

a 74.6% increase in the number of analgesics prescriptions written between 2002 and 2010, especially in the 18–49 age bracket (Jones, 2012), and narcotic analgesics were involved in more than 40% of fatal overdose deaths⁴ in the past few years (Franklin, 2012; Ruhm, 2017), statistics that contribute to the negative image associated with the use of narcotic analgesics.

Thus, it is of benefit for professionals working with those who misuse substances to have a working understanding of the narcotic analgesics, their potential benefits, and the consequences of their misuse. To assist in this process, this chapter will be split into two sections. In the first section, the use of narcotic analgesics within the medical setting will be discussed. In the second half of the chapter, the opioid use disorders (OUDs) will be discussed.

A Short History of the Natural and Synthetic Opioids

At some unknown point, it was discovered that if you made an incision on the top of the *Papaver somniferum* plant during a brief period in its life cycle, the plant would extrude a thick resin that had medicinal value. Anthropologists now believe that opium has been in use as an analgesic for at least 3,500 years, and there is evidence that the opium poppy was cultivated as a crop 10,000 years ago (Jaffe & Strain, 2005; Walton, 2002). Whether the poppy was in fact cultivated to obtain opium 10,000 years ago is not known; however, the evidence of the early cultivation of opium does hint at this possibility. For the greater part of history, opium was the mainstay in the treatment of pain,⁵ as evidenced by the fact that the English word *opium* can be traced to the Greek word *opion*, which means “poppy juice” (Stimmel, 1997a). In many cultures, opium was viewed as a gift from the gods because of its many uses: It could be used to control pain as well as severe diarrhea from conditions such as **dysentery**,⁶ for example; it had some anxiolytic properties and just plain made the user feel good.

During the chemical revolution that began in the 19th century, this resin was found to contain “an elaborate cocktail containing sugars, proteins, ammonia, latex, gums, plant wax, tars, sulfuric acid and lactic acids, water, meconic acid,

¹See Glossary.

²The last year for which statistics are available at the time of publication.

³It is of interest to note that the International Narcotics Control Board (2008), an agency funded by and a part of the United Nations, stated that: “[the] diversion of narcotic drugs from the licit to the illicit market are virtually non-existent” (p. iii).

⁴ Either alone, or in combination with other compounds.

⁵As will be discussed in Chapter 16, once aspirin was introduced, the use of narcotic analgesics for mild pain fell into disfavor.

⁶See Glossary.

and a wide range of alkaloids” (Booth, 1996, p. 4). In 1806, a chemist by the name of Friedrich W. A. Serturner isolated a compound in opium that would later be determined to be its most active ingredient (Gutstein & Akil, 2006). Because it could make the user feel tired, this alkaloid base was named *morphine* after the Greek god of dreams, Morpheus. As scientists explored the properties of morphine, it was discovered that morphine is one of 20 distinct alkaloid compounds produced by the opium poppy, but that it is a waste product produced by the plant. Where opium had been used for centuries for its analgesic properties, morphine itself was found to be about 10 times as potent as opium (Gutstein & Akil, 2006; Heyman, 2009). Another alkaloid compound isolated from the poppy was codeine, which was first isolated in 1832 and which will be discussed in more detail later in this chapter (Gutstein & Akil, 2006; Jaffe & Strain, 2005).

In 1857, about a half century after morphine was isolated, Alexander Wood invented the hypodermic needle. This device made it possible to rapidly and relatively painlessly introduce compounds such as morphine directly into the body. By the time of the Civil War in the United States, both the hypodermic needle and morphine were freely available for a modest price, without prescription. Morphine was widely used for medicinal purposes after this point, and often was a hidden ingredient in many “patent” medicines⁷ sold without prescription in the United States during the 19th century. These compounds were often sold under brand names that, to the unsophisticated person at least, gave them an aura of authenticity as medicinal compounds (Rasmussen, 2008). Surprisingly, research has found that the vast majority of physicians recommended their use at least on occasion (Rasmussen, 2008). The unregulated use of morphine as a hidden ingredient in various elixirs, plus its extensive use on the battlefield and in military hospitals, combined with the recently invented intravenous needle, all contributed to an epidemic of narcotics addiction in the late 19th and early 20th centuries. A complicating social phenomenon was the practice of opium smoking, which had been introduced into the United States on a large scale by Chinese immigrants. The result of these disparate forces was that by the year 1900 *more than 4%* of the entire population of the country was addicted to opium or other narcotics (Brust, 2004).

Faced with this growing epidemic of unrestrained narcotic misuse, the U.S. Congress passed the Pure Food and Drug Act of 1906. This law required that manufacturers list the ingredients of their product on the label. Suddenly,

many members of the general public could see that many of their most trusted home remedies contained one or more narcotic compounds, a discovery that contributed to the demise of the patent medicine movement. A decade later, the Harrison Narcotics Act of 1914 became law, after which point only a licensed physician or dentist could prescribe a narcotic analgesic. Historians attribute the reduction in recreational opioid use seen after the passage of this act directly to the new law, although in reality the wave of opioid addiction had peaked about a decade earlier, and the problem of illicit narcotics misuse was already on the decline. Unfortunately, the problem of narcotics misuse never fully disappeared, and these compounds have waxed and waned in popularity as drugs to misuse for the last century (Heyman, 2009). The opioids are dangerous compounds: In the 35–54 age cohort, the number of deaths from intentional or unintentional narcotic overdose exceeds those of firearms or motor vehicle accidents (Franklin, 2014). They are effective in alleviating short-term, acute pain from injury. Their long-term use in controlling chronic pain from conditions other than cancer remains controversial. This presents society with an enigma: They are both popular illicit recreational compounds and effective analgesics. In the next section, we will start to explore the medical applications of the narcotic analgesics.

I. The Medical Applications of Narcotic Analgesics

The Classification of Narcotic Analgesics

Few would dispute that morphine and many of its chemical cousins have proven of immense value in the control of acute pain. Since morphine was first isolated, chemists have developed a wide variety of compounds that have pharmacological effects similar to morphine. These compounds are classified as falling into three groups (Segal & Duffy, 1999): (a) natural opiates, which are obtained directly from the opium poppy (morphine and codeine are examples of this category); (b) semisynthetic opiates, which are chemically altered derivatives of natural opiates (heroin is an example of this category); and (c) synthetic opioids, which are synthesized in laboratories and not derived from natural opiates (methadone and propoxyphene are examples of this category of compounds). While there are significant differences in the chemical structures of the different compounds in each category, for the sake of this text, they will be referred to as either *opioids*, *opiates*, or *narcotic analgesics*, since they have very similar analgesic effects.

⁷The phenomenon of “patent” medicines in the 19th century is a topic worthy of a book in its own right, but must be mentioned only in passing here.

The Problem of Pain

The word *pain* comes from the Latin word *poena*, which means a punishment or penalty, which effectively explains why most of us try to avoid it (Chearle & Gallagher, 2006; Stimmel, 1997a). Each year in the United States approximately 100 million people experience some form of pain for which they receive a prescription for narcotic analgesics (Califf et al., 2016). In reality, there are several subforms of pain: (a) acute pain, (b) noncancer chronic (or persistent) pain, and (c) cancer-induced or related pain (Gunderson & Stimmel, 2004; Holleran, 2002). *Acute* pain is short, intense, and resolves when the cause (incision, broken bone, etc.) heals (Hollander, 2002). *Persistent* pain that is not associated with cancer results from pathological conditions in the body (neuropathic pain, for example), while *cancer-related* pain is the result of a tumor's growth or expansion (Holleran, 2002).

There are three different classes of compounds used to treat pain. General anesthetic agents are used to induce a loss of consciousness so that the person (hopefully) is unable to feel pain. Local anesthetic agents, the second category of analgesics, are used to block the nerve transmission of pain from the source of an injury to the brain. Cocaine was once extensively used in this capacity, but in the majority of cases it has since been replaced by other, safer, compounds. The third group of compounds are those that reduce or block the individual's awareness of pain within the central nervous system (CNS) without causing a loss of consciousness. There are several subforms in this category: Narcotic analgesics, which are "unsurpassed analgesic agents" (Bailey & Connor, 2005, p. 60) fall into this category, for example. An emerging class of analgesics are the new peripheral mu opioid receptor antagonists, a class of medications that reduce the individual's awareness of pain but which are more selective for the mu opioid receptor site than earlier narcotics. A third subgroup of such compounds are the over-the-counter analgesics, which will be discussed in Chapter 16.

Where Opium Is Produced

As was noted earlier, the natural and semisynthetic opioids are derived from raw opium, which is obtained from the resin of the opium poppy. The world's need for medicinal opium can be met by the opium fields of India. However, there are vast fields of opium poppies being grown in other countries, usually producing opium for the illicit market. It has been estimated that Afghanistan alone is estimated to grow two-thirds of the opium produced on this planet, all intended for the illicit narcotics trade, although Asia and Latin America produce significant amounts of opium as well (U.N. Office on Drugs and Crime, 2017). Globally, opium production did see a decrease in 2015, but, sadly, this was mostly related to

reduced crop yields in Afghanistan rather than global enforcement (U.N. Office on Drugs and Crime, 2017).

Current Medical Uses of Narcotic Analgesics

For thousands of years, opium was one of the few compounds available to treat pain (Gutstein & Akil, 2006). When morphine was first isolated in 1806, the main agent for pain control gradually switched from opium to morphine, which provided more predictable analgesia. With the advent of the chemical revolution, a large number of narcotic analgesics have been introduced, although they all work through the same general mechanism(s) and for the most part have only minor variations in potency, absorption characteristics, and duration of effect. The generic and brand names of some of the more commonly used narcotic analgesics are provided in Table 11-1.

Narcotic analgesics are used to control moderate to severe levels of pain, as well as to suppress the cough reflex, and on occasion to treat severe diarrhea. Nationally, it has been estimated that approximately 36% of the adult population in the United States used a prescription pain reliever in the past 12 months (SAMHSA, 2016). The vast majority of these people used a narcotic analgesic under the supervision of a physician for short-term pain control. However, nearly half of individuals using narcotic analgesics had been using one or more of these medications for more than two years, and one-fifth had been doing so for at least 5 years (Kelly et al., 2008). There is an emerging body of evidence suggesting that there are significant risks associated with long-term use of narcotic analgesics in the control of chronic pain that is not cancer-related (Franklin, 2014; Ray, Chung, Murray, Hall, & Stein, 2016).

The use of narcotic analgesics as an adjunct in the control of disease remains controversial, if only because persons on long-term narcotic treatment regimens tend to have multiple prescriptions. Approximately one-third of those persons using a prescribed narcotic analgesic were simultaneously taking five or more other nonopioid medications on a regular basis, as compared to one-tenth of persons not prescribed a narcotic analgesic (Kelly et al., 2008). The reason(s) for and the implications of this disparity are not known at this time.

Pharmacology of the Narcotic Analgesics

Morphine remains the gold standard against which the effects of any narcotic analgesic are measured. Yet morphine appears to provide a greater level of analgesia to men compared to women (Doyle & Murphy, 2017). Narcotic analgesics

TABLE 11-1 Some Common Narcotic Analgesics*

Generic Name	Brand Name	Approximate Equianalgesic Parenteral Dose
Morphine	—	10 mg every 3–4 hours
Hydromorphone	Dilaudid	1.5 mg every 3–4 hours
Meperidine	Demerol	100 mg every 3 hours
Methadone	Dolophine	10 mg every 6–8 hours
Oxymorphone	Numorphan	1 mg every 3–4 hours
Fentanyl	Sublimaze	0.1 mg every 1–2 hours
Pentazocine	Talwin	60 mg every 3–4 hours
Buprenorphine	Buprenex	0.3–0.4 mg every 6–8 hours
Codeine	—	75–130 mg every 3–4 hours**
Oxycodone	Tylox	Not available in parenteral dosage forms

*This chart is for comparison purposes only. It is not intended to serve as, nor should it be used as, a guide to patient care.
**It is not recommended that doses of codeine above 65 mg be used because doses above this level do not produce significantly increased analgesia and may result in increased risk of unwanted side effects.

SOURCE: Based on information contained in Thomson PDR (2011) and Cherny and Foley (1996).

achieve their pain-suppressant effects through one or more mechanisms: (a) inhibition of pain signals from the spinal cord to the brain, while (b) activating pain-suppression systems in the brain and spinal cord, and (c) altering the person's perception of and emotional response to their perceived pain (Savage, Kirsh, & Passik, 2008). Narcotic analgesics achieve these effects by their ability to mimic the effects of endogenous opioid peptides known as the *enkephalins*, *endorphins*, and *dynorphins* (Gutstein & Akil, 2006; Schuckit, 2010b). These natural opioid peptides function as neurotransmitters in the brain and spinal cord, especially in the hypothalamus.

Each family of opioid peptides is found mainly in a specific region of the brain, although there is a degree of overlap (Jaffe & Strain, 2005).⁸ These endogenous opioids are involved in such activities in the CNS as moderation of the emotions, anxiety, sedation, appetite suppression, and the reward cascade, and they seem to have an anticonvulsant effect. Endogenous opioids are also involved in the process of smooth muscle motility and regulation of various body functions such as temperature, cardiac rate, respiration, and blood pressure. The opioid peptides (and narcotic analgesics) affect the activity of a wide range of primary and secondary neurotransmitters such as norepinephrine, serotonin, acetylcholine, adenosine, glutamate, the endogenous cannabinoid receptors, nitric oxide receptor sites, thyrotropin releasing

hormone (TRH), and histamine. As this list would suggest, the endogenous opioids are quite powerful compounds. For example, the endogenous opioid peptide beta endorphin (β -endorphin) is, on a per-milligram basis, estimated to be 200 times as potent as morphine.

Narcotic analgesics function as opioid peptide agonists, occupying the endogenous opioid receptor site(s) to simulate or enhance the effects of these naturally occurring compounds (Reed, Picetti, Butelman, & Kreek 2015; Vanderah, 2006). A number of these receptor sites have been identified in the brain, and their distribution patterns have been mapped. Researchers have used Greek letters such as mu, kappa, and delta to identify different endogenous opioid receptor sites. Many of these receptor sites in turn have subtypes: *mu* receptor subtypes, *kappa* receptor subtypes, and *delta* receptor subtypes, for example (Jenkins, 2007; Reed et al., 2015). The primary functions of the known endogenous opioid receptor types are reviewed in Table 11-2.

There is much to be discovered about the impact of narcotic analgesics on normal brain function. There is strong evidence that when used at therapeutic doses, the narcotic analgesics alter the blood flow pattern within the brain, as evidenced by the results of the process of single photon emission computed tomography (SPECT) scan studies (Schuckit, 2006a; Schlaepfer et al., 1998).

The effects of drug-induced mu opioid receptor activation are dose-related, and include respiratory depression, cognitive blurring, constriction of the pupils, urinary retention, and at high doses the activation of the brain's reward system (Savage et al., 2008; Stahl, 2008). Activation of the kappa receptor site appears to induce less analgesia than is seen when

⁸The specific pattern of neurotransmitter distribution in the brain, and those regions where these endogenous opioid receptor sites overlap, is beyond the scope of this text. The reader is referred to a good neuropharmacology text, if s/he is interested in learning more about this phenomenon.

TABLE 11-2 Opioid Brain Receptors and Their Function

Receptor Subtype	Function in Central Nervous System
Mu (subtype 1)	Analgesia
Mu (subtype 2)	Gastrointestinal motility, bradycardia, respiratory depression
Delta	Analgesia (at level of spinal cord), constriction of pupils, sedation, minor changes in psychomotor function
Kappa	Analgesia (at level of spinal cord), sedation, respiration suppression, psychotic symptoms, reduced GI motility, dysphoria, gag reflex
Sigma	Dysphoria, hallucinations, decreased respiration, some increase in psychomotor activity levels
Epsilon	Function unknown at this time
Lambda	Function unknown at this time
Orphan opioid-like receptor-1 (ORL-1)	Function unknown at this time

SOURCES: Table based on information provided in Barnett (2001); Jaffe and Jaffe (2004); Katz (2000); Knapp, Ciraulo, and Jaffe (2005); Stout (2009); Schuckit (2006a, 2010b).

the mu receptor site is activated, and medications that bind to this receptor site thus are effective only for mild to moderate levels of pain (Savage et al., 2008). For reasons that are not clear, the kappa endogenous opioid system seems to function as an antagonist to the mu receptor system: Activation of the kappa receptor site negates any analgesia achieved by activation of the mu receptor site (Savage et al., 2008).

The subjective effects of a single dose of a narcotic analgesic are different for persons experiencing pain as opposed to those who are not experiencing significant levels of pain. Volunteers who are not in pain and who have received therapeutic doses of narcotic analgesics usually report experiencing a feeling of **dysphoria**⁹ and rarely report a degree of euphoria (Schuckit, 2006a). This would appear to reflect the activation of the sigma and kappa receptors when the pain recognition system is not active. Any sense of euphoria is thought to be caused by the effects of these compounds on the ventral tegmental region in the brain (Schuckit, 2006a). This region of the brain is rich in dopamine receptor sites, and is connected with the limbic system, both regions of the brain involved in the reward cascade. Narcotic analgesics bind to what are known as interneurons, which inhibit dopamine production in the central nervous system through the production and release of the inhibitory neurotransmitter **GABA**,¹⁰ especially in the limbic reward system (Savage et al., 2008). Without GABA neuron inhibition, the limbic reward system produces large amounts of dopamine, triggering the reward system in the brain (Savage et al., 2008). The chronic administration of morphine or similar pharmaceuticals

causes dopamine-utilizing neurons to shrink in volume by about 25% (Sklair-Tavron et al., 1996). This appears to parallel reports from persons taking a narcotic analgesic of a reduced sense of euphoria over time. In addition, persons taking prescribed narcotic analgesics have been found to be at a 35% higher risk for the development of a cardiac condition known as atrial fibrillation (Qureshi et al., 2015).

The amygdalae (singular: **amygdala**¹¹) regions of the brain have large numbers of opioid receptor sites. Currently, it is thought that the amygdalae will release endogenous opioids in response to sensory data, which influences the formation of emotionally laden memories (Jaffe & Strain, 2005). The sense of joy and accomplishment that one feels when s/he finally solves a complex math problem, for example, is the result of the amygdala's release of endogenous opioid neuropeptide molecules, making it more likely that the student will remember the solution to that problem if s/he should encounter it again. The amygdala is also involved in the initiation of the "fight or flight" response, and thus it is not surprising to learn that the endogenous opioids also play a role in dampening the fear response (Motluk, 2008).

In an animal research study involving genetically engineered mice that did not produce any of the neurotransmitter serotonin, Zhao et al. (2007) concluded that there was no apparent analgesic effect from the narcotic analgesics administered to the mice, suggesting that the serotonin neurotransmitter system is somehow involved in analgesia through an unknown mechanism. As the above information demonstrates, there is still a great deal to be learned about how the narcotic analgesics impact the normal function of the human

⁹See Glossary.

¹⁰See Glossary.

¹¹See Glossary.

brain. In the section below, we will look at some of the pharmacological properties of the more commonly prescribed narcotic analgesics.

BUPRENORPHINE

Buprenorphine is a synthetic opioid introduced into clinical use in the 1960s. As an analgesic, it is well absorbed through intramuscular and intravenous injections, and it is estimated to be 25–50 times as potent as morphine (Fudala & O'Brien, 2005; Karch, 2009). A standard conversion formula is that 0.3 mg of intravenously administered buprenorphine is approximately as powerful as 10 mg of morphine. However, the analgesic potential of this medication is limited and it has a slow onset of action. These characteristics, plus its long elimination half-life (up to 37 hours), are reasons why it is rarely used pain medication (Baron, Garbely, & Boyd, 2009; U.S. Department of Health and Human Services, 2004). Recent research suggests a possible application of this medication in controlling suicidal thoughts, although this is based only on preliminary research which must be replicated (Locklear, 2016).

Approximately 95% of the buprenorphine in the blood is protein-bound. It is biotransformed in the liver, with 79% being excreted in the feces and only 3.9% being excreted in the urine. Surprisingly, animal research suggests that the various buprenorphine metabolites are unable to cross the blood-brain barrier, suggesting that the analgesic effects of buprenorphine are induced by the molecules of the parent compound that cross over into the brain. Once in the brain, buprenorphine functions as a partial mu receptor agonist, but with some interesting properties that will be discussed in Chapter 33 (Wilson, Shannon, & Shields, 2017). It is a powerful narcotic analgesic, which unfortunately is gaining popularity as a drug to misuse.

CARFENTANIL

This is a chemical cousin to fentanyl (discussed below). It is estimated that this compound is 10,000 times as potent as morphine, and it is sold under the brand name of Wildnil®. This medication is normally used in veterinary practice to immobilize large animals (Karch, 2009). It is not intended for human use, yet this substance is contributed to an increase in overdoses and at least two deaths in North America in 2016 (U.N. Office on Drugs and Crime, 2017).

CODEINE

This is an alkaloid compound, found in the milky sap from the *Papaver somniferum* plant bulb, which was first isolated in 1832 (Gutstein & Akil, 2006). Codeine is a prodrug: About 10% of the codeine administered is biotransformed into morphine as an intermediate stage of the biotransformation process (Brunton, Parker, Blumenthal, & Buxton, 2008; Gutstein & Akil, 2006). The analgesic potential of codeine

is estimated as being about one-fifth that of morphine, but it is unpredictable due to individual variations in absorption and biotransformation (MacDonald & MacLeod, 2010). Codeine is usually administered orally. It is used to control mild to moderate levels of pain, severe cough, severe diarrhea, and on rare occasions as an anxiolytic.

Although it has been used to control mild to moderate levels of pain for more than 200 years, scientists are only now starting to study the pharmacokinetics of codeine. Following a single dose, the peak blood levels are seen in 1–2 hours, and the half-life is thought to be between 2.4 and 3.6 hours (Gutstein & Akil, 2006; Karch, 2009; Stout, 2009). It has been found that the analgesic potential of codeine is enhanced when it is mixed with over-the-counter analgesics such as aspirin or acetaminophen, and it is commonly mixed with such compounds in tablet form (Gutstein & Akil, 2006).

Codeine is biotransformed in the liver. Unfortunately, a genetic mutation found in 7–10% of Caucasians, 5% of persons of Asian descent, and 1% of persons of Middle Eastern descent inhibits their body from biotransforming codeine into morphine. As a result of this genetic mutation, these individuals obtain little if any analgesia from codeine, and require longer than normal to biotransform and eliminate this compound (Birmingham, 2017; Brunton et al., 2008; Goldstein, 2005; Stout, 2009; Zevin & Benowitz, 2007). There have also been reports of life-threatening respiratory depression in adults and in two children prescribed codeine following a routine tonsillectomy (MacDonald & MacLeod, 2010). Caution, particularly in use with children, is encouraged (Birmingham, 2017). Use in children was restricted as of 2017, as well as in pregnant women (U.S. Food and Drug Administration, 2017). Other known side effects include possible itching, nausea, vomiting, dry mouth, miosis, urinary retention, diminished libido, and possible allergic reactions.

Because they compete for the same metabolic pathway through which codeine is biotransformed, the selective serotonin reuptake inhibitors paroxetine and fluoxetine, the antidepressant bupropion, and the antihistamine diphenhydramine block the conversion of codeine into morphine and thus codeine's effectiveness as an analgesic. Unfortunately, there is much to learn about this compound and the ways in which it should be used in modern medicine (Birmingham, 2017).

FENTANYL

Fentanyl is a synthetic opioid, introduced into the United States in 1968. It offers several advantages over traditional narcotic analgesics, and is especially popular during and immediately after surgery (Wilson, Shannon, & Shields, 2011). It is well absorbed from muscle tissue, allowing for intramuscular injection, and also is well absorbed following

intravenous injection. Unlike morphine, it does not stimulate the release of large amounts of histamine, an important consideration in some cases (Brunton et al., 2008; Gutstein & Akil, 2006).

Fentanyl is quite lipid-soluble, a characteristic that makes it possible to be absorbed into the body through the skin. One common method of fentanyl administration for chronic pain is through a transdermal patch. Unfortunately, therapeutic levels of fentanyl will not build up for 12 hours after a transdermal patch is applied, a characteristic that requires the use of more traditional narcotic analgesics in the first 12 hours following application of the patch.

Fentanyl is quite potent, although there remains some controversy as to the relative potency of this compound as compared with morphine. Various researchers have estimated that fentanyl is 10 times (Greydanus & Patel, 2005), to perhaps 50–100 times as potent as morphine (Gutstein & Akil, 2006; Karch, 2009; U.N. Office on Drugs and Crime, 2017; Zevin & Benowitz, 2007). A typical intravenous dose is 1 microgram.¹² It is highly lipid-soluble, with 80% binding to lipid molecules in the blood after intravenous administration, and it reaches the brain rapidly after intravenous administration, providing analgesia in a matter of minutes after intravenous administration.

The biological half-life of a single intravenous dose of fentanyl is 1–6 hours, depending on the individual's biochemistry.¹³ Most physicians use the average figure of 3 hours when planning for the person's analgesia. When it is administered intravenously, the analgesic effects of fentanyl peak in 5 minutes and last for 30–120 minutes, both important considerations when planning the person's post-surgical analgesia (Brunton et al., 2008). It is rapidly biotransformed in the liver and excreted by the body in the urine (Karch, 2009). Unfortunately, fentanyl suppresses respiration for longer than it induces analgesia, a characteristic that physicians must keep in mind when planning for postsurgical analgesia (Wilson et al., 2011).

Between 3 and 10% of persons who receive a therapeutic dose of fentanyl will experience some degree of somnolence and/or confusion, drug-induced anxiety, hallucinations, and/or feelings of depression (Brown & Stoudemire, 1998). Approximately 1% will experience some degree of paranoia, agitation, and/or drug-induced amnesia. Other identified side effects include blurred vision, euphoria, nausea, vomiting, dizziness, delirium, and constipation (Wilson et al., 2011). Fentanyl can cause a 20% drop in the person's blood pressure,

and it can also induce up to a 25% reduction in cardiac rate. Thus, as with all compounds, the attending physician must weigh the potential benefits of fentanyl use against the possible dangers inherent in its use.

HEROIN

Technically, heroin is just two morphine molecules joined by an oxygen molecule, thus yielding its chemical name: diacetylmorphine (Brunton et al., 2008). As an analgesic, it is thought to be approximately twice as potent as morphine, and a standard conversion formula is that 10 mg of morphine has the same analgesic potential as 3 mg of diacetylmorphine (Brust, 2004). Its major first-stage metabolite¹⁴ is 6-monoacetylmorphine (6-MAM), which is then broken down into morphine. The importance of this metabolite is that it crosses over the blood-brain barrier much more quickly than does morphine itself (Gutstein & Akil, 2005). In the United States, heroin has no recognized medical use and is classified as a Schedule I substance¹⁵ under the controlled Substances Act of 1970 (Jenkins, 2007). It remains a recognized pharmaceutical in some other countries, and is used by physicians to treat severe pain.¹⁶ There is an emerging body of evidence suggesting that heroin might have a cardioprotective potential during periods of cardiac ischemia, although the exact mechanism for this is not clear at this time (Gutstein & Akil, 2006; Mamer, Penn, Wildmer, Levin, & Maslansky, 2003; Peart & Gross, 2004). This effect, if supported in future research, may make diacetylmorphine of value in treating heart attack victims; however, there is a need for further clinical research to identify the mechanism that causes this effect. Heroin as a drug that is misused in the United States will be discussed later in this chapter.

HYDROCODONE/HYDROMORPHONE

Hydrocodone is a semisynthetic narcotic derived from codeine, although it is more toxic than the parent compound. It is used to control coughs, and mild to moderate levels of pain. Technically it is a **prodrug**,¹⁷ and most of its analgesic effects are thought to reflect the action of a metabolite, hydromorphone. Hydromorphone is also a substance used in medicine, similar to hydrocodone, but derived from morphine. Orally administered doses of hydromorphone are thought to be 5–7 times as potent as orally administered morphine, although in individuals who misuse opioids its

¹²Which is about 1/60,000th the weight of a postage stamp.

¹³Some individuals will be “fast” metabolizers, while others will be “slow” metabolizers.

¹⁴As with many compounds, heroin biotransformation goes through a number of stages.

¹⁵See Appendix 3.

¹⁶Obviously, the heroin used for medicinal purposes in medical centers overseas is produced by pharmaceutical companies under controlled conditions, producing a medication of known potency and purity. The only thing that this heroin has in common with illicit heroin is its name.

¹⁷See Glossary.

potency might be reduced to approximately half this figure due to the development of tolerance (Stout, 2009). Intravenously administered doses of hydromorphone have a rapid onset of analgesia (5 minutes), and provide 3–4 hours analgesia. The elimination half-life is thought to be approximately 2–3 hours (Stout, 2009). Orally administered doses are subject to the first-pass metabolism effect. Side effects can include dizziness, sedation, mental confusion, anxiety, fear, nausea and/or vomiting, dysphoria, and respiratory depression (Alattar & Scharf, 2008). Persons receiving exceptionally large doses may also experience allodynia and possible seizures (Stout, 2009).

MEPERIDINE

Meperidine was once recommended for the treatment of persistent pain. Because many of the metabolites of this compound are toxic, its use in the medical setting is limited to 48 hours or less (Gutstein & Akil, 2006). The pharmacokinetics of meperidine are similar to those of morphine and will not be discussed further here.

METHADONE

Methadone is a synthetic opioid developed by German chemists in the 1930s, and later used by German physicians during World War II as a substitute for morphine (Traub, 2009). Although it is a useful pharmacological agent, there is a great deal of confusion surrounding this compound. It is used as an analgesic, especially in cases where the person has persistent pain that requires long-term pain control (Toombs & Kral, 2005). However, because of its utilization in *methadone maintenance programs* (also referred to as *medication-assisted treatment* when it also includes support services),¹⁸ many persons object to its use because “I’m not an addict!” To ease some of these people’s reservations about being placed on a compound that in their minds is associated with opioid use disorder, the brand name form of methadone known as Dolophine® is often prescribed (Lipman, 2008; Schuckit, 2006a).

The methadone molecule is structurally similar to the morphine molecule, and as an analgesic it is about as potent as morphine (Stout, 2009). It is well absorbed from the gastrointestinal tract, with about 80% of a single oral dose being absorbed into the person’s body (Lipman, 2008). It is also well absorbed from muscle tissue when administered in an intramuscular injection; it can also be injected subcutaneously and may be administered intravenously (Toombs & Kral, 2005). Because of its long therapeutic half-life, it can provide extended periods of analgesia and reduce “breakthrough” pain episodes, which can cause distress in the patient. In the

opiate-naïve person, analgesia is usually achieved with small oral doses of methadone (5–20 mg two to four times a day).

Methadone is highly lipophilic, and once in the circulatory system is rapidly distributed to blood-rich organs such as the brain, liver, lungs, and kidneys. The analgesic effects of oral doses of methadone begin within 30–60 minutes, peak about 2–4 hours after the dose is administered, and continue to be effective for 4–6 hours depending on the individual’s biochemistry (Lipman, 2008). Repeated doses of methadone provide a reservoir of methadone to build up in the body, which is then slowly released back in the circulation over time, providing a relatively steady blood level in the person’s blood. However, methadone provides a prime example of how the therapeutic half-life might be shorter than the elimination half-life. In contrast to the therapeutic half-life, the elimination half-life of methadone is between 13 and 58 hours, and depending on the individual’s biochemistry, might possibly be as long as 128 hours in methadone-naïve users who have not developed tolerance to the compound (Schottenfeld, 2008). The speed at which methadone is eliminated from the body is dependent upon the individual’s biochemistry and the acidity level of the individual’s urine (Drummer & Odell, 2001; Karch, 2009). If the individual’s urine is very acidic, the elimination half-life of a single dose of methadone is reduced by 50% (Drummer & Odell, 2001). When administered over extended periods of time to treat persistent pain, the methadone biotransformation period becomes shorter, reducing the elimination half-life to around 48 hours (Schottenfeld, 2008).

The toxicity of methadone varies from individual to individual, with doses of 50 mg or less proving to be fatal to nontolerant adults in some cases, while doses of 180 mg/day are often used in methadone maintenance programs. The potential for a lethal overdose is higher in children who accidentally obtain this medication, with doses as low as 5–10 mg having been fatal to children in some cases (Schottenfeld, 2008).

The major route of biotransformation is through the liver, and the process of methadone biotransformation produces nine different metabolites, none of which appear to have any analgesic potential of their own (Lipman, 2008; Stout, 2009). The majority of these metabolites are excreted in the bile (Lipman, 2008). When used to treat non-cancer pain, it is recommended that the patient be started at very low doses to avoid respiratory distress, after which the dose can be slowly increased every 4–5 days to avoid inducing respiratory depression and possibly death (Lipman, 2008). However, because of this, it might take up to 12 days of dosage adjustments before the person achieves a steady-state level of methadone and thus optimal levels of analgesia (Chou et al., 2009).

¹⁸Which will be discussed in Chapter 33.

As is true for its chemical cousin morphine, tolerance to the effects of methadone develops unevenly. The patient might quickly become tolerant to the euphoric effects of methadone, while tolerance to the gastrointestinal effects (constipation) might develop slowly if at all (Lipman, 2008). Tolerance to the respiratory depression effects of methadone is incomplete, and the long elimination half-life of methadone can place placing the person at risk for respiratory depression for extended periods of time after discontinuing use of methadone (Baron et al., 2009). Sensitivity to the respiratory depressant effect of methadone might be magnified by the concurrent use of other CNS depressants such as alcohol or other pharmaceuticals. Further, neuroadaptation to the effects of methadone are rapidly reversed after abstinence, so that if the person should resume this medication after a period of abstinence, it will be necessary to slowly increase the daily dose until the patient achieves the desired degree of analgesia (Lipman, 2008).

This compound does present some other unique dangers. Methadone can induce cardiac arrhythmias when used at therapeutic doses (Chou et al., 2009; Wedam, Bigelow, Johnson, Nuzzo, & Haigney, 2008). It is thought that methadone can prolong the QT interval¹⁹ of the normal heart rhythm and induce a potentially fatal arrhythmia known as **torsade de pointes** (Chugh et al., 2008; Schottenfeld, 2008; Webster et al., 2011). The causal mechanism appears to be methadone's ability to block the normal action of the potassium channels in the cardiac heart muscles, which are required for the rapid repolarization of the muscles for the next heartbeat (Malik & Stillman, 2009). Between 10 and 15% of those people on methadone who develop this arrhythmia are thought to have a subclinical form of **ventricular tachycardia**,²⁰ which is then exacerbated by methadone.²¹ The exact percentage of persons on methadone who go on to develop torsade de pointes is thought to be <1%, but physicians are advised to assess the person for this possible drug complication through the use of serial electrocardiogram (EKG) studies, since the mortality rates of these cardiac problems is so high.

In recent years, the media have focused attention on the "epidemic" of methadone-related deaths. While this is not to ignore the dangers associated with methadone use, the concurrent use of CNS depressants such as the

benzodiazepines or even over-the-counter compounds such as antihistamines can increase the risk of an overdose (Lipman, 2008). Methadone overdoses can be treated by blocking agents such as Narcan®, but the extended half-life of methadone makes it imperative that the patient continue to repeatedly receive the appropriate dose of this antidote over extended periods of time. Methadone overdose deaths have been known to occur up to 24 hours after the individual's overdose was ingested, or after the narcotic blocker was discontinued (Schottenfeld, 2008).

When used as prescribed, methadone has a very good safety profile. Even after years of prescribed use, there is no evidence of drug-induced damage to the lungs, kidneys, liver, brain, stomach, or spleen. Unfortunately, methadone will interact with *at least* 100 different pharmaceuticals currently in use in the United States (Schottenfeld, 2004; "Taming drug interactions," 2003). Depending on the exact nature of the drug(s) involved, the methadone-drug interaction might range from inconvenient to life-threatening.²² Some of the medications that might interact with methadone include (but are not limited to): carbamazepine, phenytoin, risperidone, ritonavir, and the herbal medication St. John's wort, all of which may reduce the person's blood methadone levels. Other medications such as fluoxetine, fluvoxamine, saquinavir, cimetidine, erythromycin, and ciprofloxacin may slow the rate of methadone biotransformation, causing higher than normal (possibly fatal) blood levels of the latter compound (Drummer & Odell, 2001; "Methadone-cipro interactions," 2002; Schottenfeld, 2004). Persons taking methadone should avoid the use of other CNS depressants such as alcohol or antihistamines to avoid a potentially fatal potentiation effect between the chemicals being abused. This is one reason why individuals who misuse multiple drugs are at increased risk for a potentially fatal overdose. For example, there is one known case report of a fatal drug interaction effect for a person taking both methadone and a benzodiazepine (Schottenfeld, 2008). There is also evidence that methadone might interfere with the antithrombotic action of aspirin, thus allowing the blood to form clots more easily, possibly contributing to a heart attack, stroke, or other serious medical problem (Malinin, Callahan, & Serebruany, 2001). While this list of potential drug interactions is far from being comprehensive, it does illustrate the potential for potentially fatal drug interactions between methadone and a wide range of other compounds.

¹⁹Technically the time required for the activation and then recovery from a single heartbeat on an electrocardiogram.

²⁰See Glossary.

²¹It is important to keep in mind that ventricular tachycardia has a number of causes, not just the use of methadone.

²²As always, persons on any prescribed medication should consult with a physician or pharmacist before taking either another prescribed medication, or, an over-the-counter product.

MORPHINE

The resin that is collected from *Papaver somniferum* as the poppy head is lanced at the proper time contains 10–17% morphine (Brust, 2004; Jenkins, 2007; Jenkins & Cone, 2008). Morphine was first isolated more than 150 years ago, but it still remains the gold standard against which other narcotic analgesics are measured (D'Arcy, 2005; Gutstein & Akil, 2006; Traub, 2009).

Morphine can be administered orally and is rapidly absorbed through the gastrointestinal tract. However, between 60 and 80% of a dose of morphine will be biotransformed by the **first-pass metabolism**²³ effect before it reaches the brain (Stout, 2009). This makes orally administered doses of morphine of limited value in treating severe pain. A standard conversion formula is that 10 mg of injected morphine induces the same level of analgesia as 60 mg of orally administered morphine (Cherny & Foley, 1996). This, plus the fact that it is well absorbed from both intramuscular and intravenous injection sites, results in the usual routes of administration being intramuscular or intravenous injections. A rare but effective route of administration is rectal suppositories. This takes advantage of the fact that morphine is easily absorbed through the mucous membranes of the body such as those found in the rectum. However, this method of morphine administration is so rare that it will not be discussed again in this text.

The peak blood levels after a single dose of morphine are achieved in about 60 minutes after an oral dose, and within 30–60 minutes following intravenous injection (Wilson et al., 2011). After absorption into the body, about one-third of the morphine will become protein-bound, providing a reservoir of yet-to-be-metabolized morphine in the body for several hours. This is an advantage because the unbound morphine molecules will be rapidly distributed to every blood-rich organ, including the lungs, muscle tissues, kidneys, liver, spleen, and brain. The analgesic effects of a single dose of morphine last approximately 4 hours (Gutstein & Akil, 2006). The biotransformation half-life of a single dose of morphine ranges from 1 to 8 hours depending on the individual's biochemistry, with most textbooks offering an average figure of 2–3 hours (Drummer & Odell, 2001). Morphine crosses through the blood-brain barrier slowly, taking between 20 and 30 minutes to accomplish this task, and thus the analgesic effects of morphine might require as long as a half hour to reach full effect.

The majority of the morphine is broken down into the metabolite *morphine-3-glucuronide* (M3G). A smaller amount will be biotransformed into *morphine-6-glucuronide*

(M6G), and the remainder is biotransformed into one of several additional metabolites (Brunton et al., 2008; Karch, 2009). Interestingly, M6G has a stronger analgesic effect than its parent compound (Wynn, Oesterheld, Cozza, & Armstrong, 2009). When morphine is administered on a repeated basis, the analgesic effect of M6G has been estimated to reach between 2 and 20 times that of morphine itself, possibly accounting for morphine's analgesic effects in such cases (Gutstein & Akil, 2005; Wynn et al., 2009). The elimination half-life of morphine is thought to be between 2 and 3 hours, but is slightly longer in men than in women (Lipman, 2008).

OXYCONTIN

OxyContin was introduced in 1995 as a time-released form of oxycodone, itself a synthetic opioid. It was designed for use in cases where the patient was suffering moderate to severe long-term pain that could be controlled by oral medications. There are two forms of OxyContin: standard and controlled-release forms. Peak blood levels are achieved in about 1 hour when the regular form is ingested, or in about 3 hours when the extended-release form is ingested by the patient. It is recommended that the patient be started on 10 mg of the controlled-release form every 12 hours, a dosage level that may be adjusted by the physician to achieve optimal pain control.

The mechanism by which oxycodone produces analgesia is still in dispute. Some researchers have suggested that it is a kappa opioid receptor agonist, while others dispute this claim on the grounds that its effects are so similar to those of other opioid mu receptor agonists. After a single oral dose, peak blood levels are achieved in about an hour, and its duration of effect is approximately 12 hours. Relatively stable blood levels of OxyContin are reached after 2–3 doses, providing better pain control than could be achieved using short-acting narcotic analgesics (Borg et al., 2014). Unfortunately, OxyContin has become a major drug to misuse, which will be discussed later in this chapter.

OXYMORPHONE

Oxymorphone has reappeared on the market after an earlier version, Numorphan®, was removed from the market in the 1970s, in part because of its history of being misused. This compound was reintroduced in 2006 in both immediate-release and timed-release forms under the brand name of Opana®. When injected, this compound is thought to be about 10 times as potent as morphine. The manufacturer attempted to gain approval from the Food and Drug Administration (FDA) to market this compound in 2003, but the application was rejected by the FDA on the grounds that the drug did not appear to be effective enough, and because several patients had overdosed on the medication following

²³Discussed in Chapter 3 and in the Glossary.

surgery. Not surprisingly, company-sponsored research studies found that Opana (oxymorphone) *was* effective (Peniston & Gould, 2009) and a new application for medication approval was accepted. The statistical methodology used in these studies has been challenged, in part because the methodology allowed the researchers to weed out those persons who did not respond well to the drug from being included in the study. Although the manufacturer has attempted to introduce formulations of this compound that would discourage individuals from misusing it, individuals who seek to misuse it have already developed techniques to negate these anti-misuse formulations and have been misusing this compound through intravenous injection. Questions have been raised as to whether there is a need for a new narcotic analgesic that essentially duplicates the effects of other, established, compounds in this class, especially since individuals have suffered such side effects as interference with the body's blood clotting system and permanent damage to the heart, lungs, and kidneys. The fact that individuals who seek to misuse this substance have found ways to negate anti-misuse formulations so that they might inject this compound suggests that it has a high potential for misuse, raising additional questions about the need for yet another narcotic analgesic of this class.

PROPOXYPHENE

This is a synthetic narcotic analgesic that is almost as effective an analgesic as codeine (Graedon & Graedon, 1996). It was widely prescribed for mild to moderate levels of pain, often in combination with over-the-counter analgesics such as acetaminophen. It was introduced as having little misuse potential, but within a short time of its introduction, "dependence and abuse became a problem of epidemic proportions" (Breggin, 2008, p. 397). In February 2009, an advisory panel to the FDA recommended that production of this compound be discontinued and that it be removed from the market. The FDA initially rejected this recommendation; however, the discovery that propoxyphene could cause cardiac arrhythmias even at therapeutic dosage levels resulted in the FDA recommending that production in the United States be discontinued in 2010. Obviously, pharmaceutical companies in other countries might continue to produce it, and propoxyphene could be smuggled into the United States. Patients might also have unused prescriptions for this medication, and so it is likely to remain available in this country for some time.

Propoxyphene is a very mild mu receptor antagonist when taken at recommended doses, and for this reason it was used for mild to moderate levels of pain. However, when taken concurrently with other CNS depressants such as alcohol, or in overdose situations, it can induce respiratory depression and possibly death. This compound has a reputation as being popular for suicide gestures, attempts,

and completed suicides ("Propoxyphene pharmacokinetics," 2009). Even when used at therapeutic doses, propoxyphene is not without its dangers. A metabolite produced during the biotransformation process, norpropoxyphene (NP), is able to induce 2.5 times the level of cardiac depression of the parent compound. As noted above, it can also cause cardiac arrhythmias. Further, the elimination half-life of NP is approximately 36 hours, or three times that of propoxyphene itself. Thus, with repeated propoxyphene doses being administered for analgesia, significant levels of NP can accumulate in the user's body. Further, propoxyphene (or its metabolite NP) inhibits the ability of the liver to biotransform a wide range of other compounds, some of which are used to control seizures ("Propoxyphene pharmacokinetics," 2009).

TRAMADOL

Tramadol is a distant chemical cousin of codeine (discussed above). It is used to treat mild to moderate levels of pain, and is thought to be of value in controlling the pain of childbirth because it induces less neonatal respiratory depression following birth (Brunton et al., 2008). As an analgesic, it is thought to be about as potent as morphine (Brunton et al., 2008). Between 70 and 75% of a single oral dose reaches the circulation, and 20% of this is protein-bound. Peak plasma levels are reached in about 2.3 hours, and the half-life is 5.5 hours following a single oral dose (Brunton, Lazo, & Parker, 2006).

Although tramadol has long been viewed as a safe narcotic analgesic for use in mild to moderate pain, Daubin and colleagues (2008) described at length the clinical course of a person who had ingested a drug overdose of various compounds, including tramadol. The authors concluded that the prescribing physician needed to be vigilant when prescribing this compound, which is possibly more toxic than originally thought. Use in children was restricted as of 2017, as well as in pregnant women (U.S. Food and Drug Administration, 2017). Of those prescribed tramadol, close to 10% misuse this substance (SAMHSA, 2016).

SUFENTANIL

This is a chemical cousin to fentanyl, and is sold under the brand name of Sufenta®. It is a pharmaceutical commonly used intravenously in cardiac surgery, and is estimated to be 1,000 times as potent as morphine (Brunton et al., 2008; Karch, 2009; U.N. Office on Drugs and Crime, 2017). The pharmacokinetics of this compound are similar to that of fentanyl.

Non-Opioid Analgesics

A new analgesic compound is ziconotide (Prialt®), a substance derived from the venom of the marine snail *Conus magus*. This compound blocks calcium channels in neurons

responsible for pain transmission signals, reducing the sensitivity of neurons involved in the process of pain recognition. This compound is not effective as a primary analgesic for acute injuries, but is of value for persistent pain conditions. It is extremely potent, and is administered through an indwelling pump. Ziconotide is capable of inducing neurological side effects including (but not limited to) blurred vision, nystagmus, ataxia, gait disturbance, sedation, drug-induced psychotic reactions, and depression that might result in suicide (Maier, Gockel, Gruhn, Krumoval, & Edel, 2011). Thus, close clinical monitoring is necessary to identify these consequences and to immediately discontinue the medication. However, for those persons who are able to benefit from this medication, it offers the hope of relief from persistent pain without the use of narcotic analgesics.

Peripheral Mu Opioid Receptor Antagonists

These are a new class of compounds, two of which, methylnaltrexone and alvimopan, were the first to be introduced in the United States (Anantharamu et al., 2015). Naloxegol was also recently approved (Anantharamu et al., 2015). These compounds are mu receptor antagonists but have poor lipid-solubility, and possess an electrical charge that inhibits their crossing the blood-brain barrier. In theory, this does not reverse opioid-induced analgesia in the CNS, but binding at mu opioid receptor sites in the intestines will reduce opioid-induced constipation, which is often a complication of the use of opioids in pain control (Anantharamu et al., 2015; Moss & Rosow, 2008). These compounds are also the first in the class of a new family of compounds that may limit, or reverse, many of the adverse effects of opioids, allowing the latter drugs to be used more effectively as analgesics. An unintended side effect of these medications, however, is that they might potentially induce the narcotic withdrawal syndrome, since their chemical structure inhibits but does not prevent them from crossing the blood-brain barrier and reaching the mu receptor sites in the brain.

Neuroadaptation to Narcotic Analgesics

Analgesia is not a static process, but is influenced by a host of factors such as (a) genetic heritage, (b) disease progression, (b) increase/decrease in level of physical activity, (c) medication compliance/noncompliance, (d) medication interaction effects, and (e) the process of neuroadaptation to the medications being used by the person. The first point, the individual's genetic heritage, is occasionally a source of some confusion in that a small percentage of the population possesses what is known as **innate tolerance**

to a narcotic analgesic (Chang, Chen, & Mao, 2007). This is observed from the very first dose of a narcotic analgesic and reflects the fact that the individual's genetic heritage is such that the individual is less responsive to some narcotic analgesics than others.

In contrast to innate tolerance is what is known as **acquired tolerance**, which reflects adaptive changes within the neurons to the presence of narcotic molecules. Neuroadaptation to narcotic analgesics is rapid but incomplete, and develops at an uneven pace (Jaffe & Jaffe, 2004). Animal research has demonstrated changes in neuronal responsiveness to an opioid after just a single dose, demonstrating the speed at which neuroadaptation begins (Bailey & Connor, 2005). There is wide interindividual variation in the speed at which neuroadaptation develops, with some persons becoming tolerant to opioid-induced analgesia after just a few days of continuous use at a set dosage level (Ivanov, Schulz, Palmero, & Newcorn, 2006). That the process of neuroadaptation is often incomplete is evidenced by the fact that persons on narcotic analgesics might never fully adapt to narcotic-induced constriction of the pupils even after extended periods of narcotic use (Schuckit, 2006a).²⁴

Unfortunately, neuroadaptation is occasionally misinterpreted as evidence of an opiate use disorder (OUD), making the physician reluctant to increase the individual's medication dosage. This condition is sometimes termed *pseudo-addiction*, as opposed to a real OUD. The differentiation between these two conditions lies in the fact that once the person's pain is adequately controlled, he or she will not request additional narcotic analgesics. Physicians have discovered that the use of *dextromethorphan*,²⁵ an NMDA receptor antagonist used to suppress the cough reflex, will slow the development of neuroadaptation and improve analgesia without the need for a dosage increase (O'Brien, 2001). It has also been found that the concurrent use of over-the-counter analgesics potentiates the effects of prescribed narcotic analgesics through an unknown mechanism (Gutstein & Akil, 2006). Thus, a dosage increase is not the only answer to the development of neuroadaptation to narcotic analgesics.

THE PROBLEM OF HYPERALGESIA

In rare cases, the neural pain receptors become sensitized, responding to noxious stimuli more strongly than normal (Vanderah, 2006). This process is not a sign of tolerance to

²⁴This rule does not apply to persons who have suffered some degree of traumatic brain injury (Schuckit, 2006a). In such cases, the individual's pupils might respond to light in a manner not seen in the normal individual.

²⁵Used in cough control agents.

the effects of the narcotic analgesic being used, but rather a neurological over-response to what would normally be a less painful stimulus. Surprisingly, in even less common cases the pain recognition system neurons might respond to normal stimuli as if it were a sign of injury, sending pain messages to the brain without an injury. This condition is known as **allodynia**, and it is exceptionally rare.

WITHDRAWAL FROM NARCOTIC ANALGESICS WHEN USED IN MEDICAL PRACTICE

Most persons who receive narcotic analgesics are able to discontinue the use of these medications without significant distress. A small percentage of such persons will develop a **discontinuance syndrome**. The discontinuance syndrome might develop in persons who receive as little as 15 mg of morphine three times a day for 3 days (Ropper & Brown, 2005). This discontinuance syndrome is usually mild and does not require treatment, although in some cases the person is advised to gradually “taper” from the medication rather than to just discontinue it, and in rare cases supportive pharmacotherapy will be needed to help relieve the person’s distress during this time.

Subjective Effects of Narcotic Analgesics When Used in Medical Practice

There are several factors that influence the effects that a narcotic analgesic will have on a person, including (a) the route of administration, (b) the interval between doses, (c) the actual dose of the medication being used, (d) the half-life of the medication being used, (e) the individual’s anxiety level, (f) their expectations for the medication, (g) the length of time that s/he has been used a given narcotic analgesic, (h) the individual’s expectations for the medication’s effects, and (i) the individual’s biochemistry. The latter point is illustrated by the earlier observation that a certain percentage of the population lack the ability to manufacture an enzyme necessary to break down codeine, and thus are unable to receive any benefit from this medication.

When used as an analgesic, between 80 and 95% of persons who receive a dose of morphine report that their fear, anxiety, and/or tension levels are lower after the medication begins to work (Brown & Stoudemire, 1998). Other descriptions include less intense pain, less discomfort, that they become sleepy, and possibly that their pain might have disappeared entirely (Knapp, Ciraulo, & Jaffe, 2005). When used to control coughing, patients report that their cough is less frequent and that they are able to get more rest. In rare circumstances, narcotic analgesics are administered to control massive diarrhea, although with the introduction of newer medications this use of opioids is rather rare.

Complications Caused by Narcotic Analgesics When Used in Medical Practice

GENERAL VULNERABILITY

There is strong evidence that the individual’s risk for developing an adverse reaction (side effect) to any of the narcotic analgesics is affected both by their genetic heritage and surprisingly by environmental factors (Angst et al., 2012). The authors found that approximately one-third of the variability in side effects such as sedation, pruritus, and dizziness appeared to reflect both genetic and environmental factors such as age, sex, race, level of education, and mood.

CONSTRICTION OF THE PUPILS

When used at therapeutic doses, narcotic analgesics cause the pupils of the eyes to become constricted (**miosis**). Some persons will experience this effect even in total darkness (Wilson et al., 2011). Some physicians interpret this as a sign of opiate addiction, although in fact it is a normal side effect of the narcotic analgesics and is occasionally seen in persons who are not taking/misusing these medications.

RESPIRATORY DEPRESSION

At therapeutic doses, narcotic analgesics make the brainstem less responsive to blood carbon dioxide levels, potentially causing some degree of respiratory depression (Brunton et al., 2008; Brust, 2004). Age is also a factor, with older individuals experiencing a greater degree of respiratory depression after using a narcotic analgesic (Angst et al., 2012). Because of this, there is an ongoing debate concerning whether narcotic analgesics can safely be used by persons with breathing disorders. Webster and colleagues (2011) noted, for example, that breathing disorders such as sleep apnea exacerbate the risk of an opioid-related death, especially in middle-aged, more obese, clients. This danger is increased with the concurrent use of other CNS depressants such as the benzodiazepines. In contrast, Estfan and colleagues (2007) suggested that if the attending physician were to increase the person’s dose in a timely and appropriate manner, there is little danger even for persons whose breathing has been compromised by disease (Estfan et al., 2007). Indeed, the danger is not so much the narcotic analgesic as it is the skill and knowledge of the prescribing physician (George & Regnard, 2007), and the narcotic analgesics are the drugs of choice if the benefits outweigh the dangers associated with their use (McNichol et al., 2003).

GASTROINTESTINAL SIDE EFFECTS

When used even at therapeutic levels, narcotic analgesics can induce nausea and vomiting, especially during the first 48 hours of treatment or a major dose increase (Barnett, 2001; Dilts & Dilts, 2005). At therapeutic doses, 10–40%

of ambulatory persons will experience some degree of nausea, and approximately 15% will actually vomit following the administration of their medication (Swegle & Logemann, 2006). This unwanted effect of narcotic analgesics appears to be most common in the ambulatory person, and patients are advised to rest after receiving a dose of medication to minimize this effect. Further, the individual's vulnerability to this effect is mediated, in part, by his/her genetic heritage, with some individuals demonstrating opioid-induced nausea or vomiting even at very low dosage levels (Brunton et al., 2008). To combat this side effect, some clinicians advocate the use of *ultra-low* doses of the narcotic blocker naloxone to block the opioid-induced nausea (Cepeda, Alvarez, Morales, & Carr, 2004).

Even at therapeutic doses, narcotic analgesics have been found to alter the normal function of the gastrointestinal tract in a number of ways. All narcotic analgesics decrease the secretion of hydrochloric acid in the stomach, and slow the muscle contractions of **peristalsis**²⁶ (Dilts & Dilts, 2005; Gutstein & Akil, 2006). This side effect is of great value in controlling the diarrhea caused by dysentery or similar disorders, but it is also a bothersome, occasionally life-threatening problem for persons receiving narcotic analgesics for pain control. The muscle contractions might slow to such a degree that patients develop constipation, or possibly even an intestinal blockage (Jaffe & Jaffe, 2004; Swegle & Logemann, 2006). Tolerance to this effect does not appear to develop even after periods of extended narcotics use (Swegle & Logemann, 2006). Mild cases might be controlled by over-the-counter laxatives (Barnett, 2001), and experimental evidence suggests that the compound methylaltrexone might relieve extreme opioid-induced constipation (Barnett, 2001; Moon, 2008b).

BLOOD PRESSURE EFFECTS

Narcotic analgesics should be used with great caution immediately following head trauma. **Edema**²⁷ in such cases is common, and if the narcotic analgesic administered to the person should reduce respiration, the heart will pump even more blood to the brain to compensate for the increased carbon dioxide levels, exacerbating cerebral edema if present.

OTHER SIDE EFFECTS

At therapeutic doses, narcotic analgesics stimulate the smooth muscles surrounding the bladder, while simultaneously reducing the voiding reflex, causing urinary retention (Brunton et al., 2008; Dilts & Dilts, 2005). Sedation, while a desired side effect in many settings, may interfere with the

individual's ability to safely handle power tools or a motor vehicle, and contribute to an increase in accidental injuries (Blondell & Ashrafioun, 2008). The initial dose(s) of a narcotic analgesic can induce transitory changes in cognition (including memory loss and/or confusional states), compounding the effects of infection(s), dehydration, metabolic dysfunctions, or late-stage cancer (Swegle & Logemann, 2006). It has been demonstrated that between 4 and 35% of persons receiving a narcotic analgesic for the control of pain will experience some degree of drug-induced irritability, and that 4–25% will experience some degree of drug-induced depression. The initial doses of a narcotic analgesic can reduce blood testosterone levels (Schuckit, 2008b). Nightmares, while well documented, have not been studied in detail. When used at high dosage levels, all narcotic analgesics can induce seizures, although this side effect is more commonly seen when these compounds are abused, since abusers are more likely to utilize the higher dosage levels generally necessary to induce seizures (Gutstein & Akil, 2006).

Preliminary evidence suggested that an unexpected side effect of narcotic analgesic use at therapeutic doses was a 200% higher risk for the user to commit a homicide (Tiihonen, Lehti, et al., 2015). The exact mechanism for these findings is unknown but may reflect a disinhibition effect induced by the narcotic analgesic. As a class of pharmaceuticals, narcotic analgesics can cause the person to become dizzy, lose their balance, and fall, possibly compounding the problem(s) for which they were taking these medications. While advancing age is a risk factor for falls and injury, even young adults are not entirely safe from this side effect. Unfortunately, an ever-increasing number of older persons are being prescribed narcotic analgesics for pain (Fauber & Gabler, 2012).

THE DANGER OF PHYSICIAN-INDUCED ADDICTION

Many health care workers will admit to an ongoing fear that they will cause the patient to become addicted to narcotic analgesics. This would be called an **iatrogenic** addiction. In reality, unless the person has a prior history of an SUD, only 1 in every 14,000 persons who receives a narcotic analgesic for the short-term control of acute pain is thought to be at risk for the development of an iatrogenic addiction. Given the higher risk for individuals with a prior history of an SUD, when such individuals are injured or require surgery for one reason or other, there arises a treatment dilemma for the attending physician(s).

A NEW APPROACH TO PAIN

For the most part, neuroscientists have ignored the possibility the possibility that the immune system plays a role in pain perception. This area of research offers the potential for new avenues for the treatment of pain. Further, Zylka and

²⁶See Glossary.

²⁷See Glossary.

colleagues (2008) has uncovered a new approach to pain, one that does not use narcotic analgesics. On the basis of animal research, the authors suggested that a previously unknown protein molecule known as prostatic acid phosphatase (PAP) helps neurons generate adenosine, a molecule known for its ability to suppress pain at the neural level. This process appears to generate a level of analgesia eight times as powerful as that achieved by morphine; it seems to be applicable to neurogenic pain as well as possibly acute pain, without the sedation seen with narcotic analgesics, for extended periods of time. Further research into this novel approach to pain control is needed, but this does offer an exciting non-opioid approach that seems promising.

Section Summary

As is evident from the above information, the narcotic analgesics are powerful compounds that have the potential to bring great benefit to the patient, but only at significant risk. The opioids, be they natural, semisynthetic, or synthetic compounds, have similar effects on the brain: They block the person's awareness of pain, bringing relief to the person at a time when s/he is in distress. However, they are not perfect compounds, forcing the person to experience any of a wide variety of side effects such as constipation, alterations in consciousness, respiratory depression, etc. Scientists continue to search for and investigate potential compounds that might produce analgesia without the side effects brought on by narcotic analgesics.

II. Opiates as Drugs of Misuse

The popular image of the individual who misuses narcotics is that of the person addicted to heroin, huddled in the corner of a building, with a belt around his or her arm, injecting heroin into a vein. Such persons make up only a small percentage of those who misuse narcotics. Surprisingly, 97% of those persons who begin to misuse prescription narcotic analgesics obtained their drug not from illicit drug dealers, but from a physician who prescribed it, or from a friend or relative who had a prescription for medications such as Vicodin® or OxyContin® (“Adult use of prescription opioid pain medications—Utah, 2008,” 2010). Unfortunately, such frivolous opiate misuse often progresses into an opioid use disorder, and only 16% of those persons with an identified opioid use disorder ever receive the treatment necessary to help them learn to abstain from narcotics (Saloner & Karthikeyan, 2015). To clarify such misunderstandings about the misuse of narcotic analgesics, the opiate use disorders will be examined in this section.

Why Do People Misuse Opiates?

At first glance, it would appear that the answer to this question is simple: They make the individual feel good.²⁸ The exact mechanism by which opioids might induce a sense of pleasure remains unknown but appears to reflect a drug-induced activation of the reward system (Gutstein & Akil, 2006; Schuckit, 2008b). Depending on the specific compound being misused, the method by which it is administered, the individual's drug use history, and the user's expectations for the drug(s) misused, the intensity of these feelings can vary from mild to such an intense feeling that it has been compared to the sexual orgasm in intensity (Jaffe & Strain, 2005; O'Brien, 2011).

The Mystique of Heroin

Heroin misuse accounts for 75% of the opioid use problem around the world, with an estimated 11.7 million persons consuming some 375 metric tons of heroin in 2009 (United Nations, 2011). It has been estimated that 9.3 million heroin users live in Asia, 3.6 million in Europe, and 1.2 million in the United States (United Nations, 2011). Approximately 80% of heroin users started with prescription opiates (White, 2017).

A SHORT HISTORY OF HEROIN

Heroin was first developed by chemists at the Bayer pharmaceutical company of Germany. The chemists who first developed this compound tried it on themselves, found that it made them feel “heroic,” and so it was given the brand name *Heroin* (Mann & Plummer, 1991, p. 26). It was introduced for commercial use in 1898. Like its chemical cousin morphine, heroin is obtained from raw opium, with 1 ton of raw opium yielding 100 kg of heroin after processing (“South American drug production increases,” 1997).

During the 19th century, large numbers of soldiers became addicted to morphine, which was freely administered to treat battlefield wounds or illness. Following its introduction, heroin was found to stop morphine withdrawal at low doses, and because of this it was initially thought to be a treatment for morphine addiction (Walton, 2002). Further, both morphine and heroin were found to suppress the coughs associated with conditions such as pneumonia and tuberculosis, both leading causes of death at that time, and were thought to be a treatment for either disorder. It was not until 12 years after its introduction that the addictive potential of heroin was generally recognized. However, by that time, heroin misuse and addiction had become a fixture in the United States.

²⁸Does anybody ever misuse a drug because it makes the feel bad?

By the 1920s, the term “junkie” was coined for individuals addicted to heroin and who supported their drug habit by collecting scrap metal from industrial dumps for resale to junk metal collectors (Scott, 1998). While the procedure(s) by which those who use heroin obtain their money has changed over the years, the process has not: Those addicted to heroin must still feed their “habit” every day. However, the face of heroin misuse and addiction is changing: Over the past generation, substance treatment professionals have observed that heroin misuse and addiction has migrated from the inner cities to the more affluent suburbs, and from what was a predominantly minority population to a growing subpopulation of Caucasians (Cicero, Ells, Surratt, & Kurta, 2014). Also, as the cost of buying pharmaceutical narcotics that have been diverted to the illicit drug trade becomes too high for some individuals, they are steered to the use of heroin as a cheaper alternative.

THE PHARMACOLOGY OF HEROIN

Essentially, heroin is a prodrug (Jenkins & Cone, 1998)—a pair of morphine molecules bonded together by an oxygen molecule. The result is an analgesic that is more potent than morphine; a standard conversion formula is that 3 mg of heroin has the same analgesic potential as 10 mg of morphine (Brust, 2004). The half-life of heroin has been estimated as between 2 and 3 minutes (Drummer & Odell, 2001) to perhaps as long as 36 minutes (Karch, 2009). Eventually, heroin is biotransformed into morphine, but an intermediate metabolite of heroin biotransformation has been found to be exceptionally lipid-soluble, allowing this metabolite to cross the blood-brain barrier up to 100 times more rapidly than morphine (Brunton et al., 2008). It would not be unreasonable to assume that this metabolite is biologically active and may have an analgesic potential in its own right. However, the current theory is that heroin’s analgesic power is the result of its breakdown into morphine (Drummer & Odell, 2001; Karch, 2009). After it has been biotransformed into morphine, its distribution and elimination patterns follow those of medicinal morphine, discussed in the first section of this chapter.

SUBJECTIVE EFFECTS OF HEROIN WHEN MISUSED

There are a number of factors that influence the subjective effects of heroin, including (a) the individual’s expectations for the drug, (b) the dosage, and (c) the method of heroin misuse. Intranasally administered heroin, for example, is poorly absorbed by the body, with only 25% of the available heroin reaching the general circulation. Once in the blood, the heroin molecules form strong chemical bonds with lipid molecules in the blood. In contrast with intranasal administration is the virtual 100% absorption rate achieved when heroin is administered intravenously. Intranasal users report achieving

a gentle sense of euphoria, in contrast to the “rush” or “flash” experience that is very similar to sexual orgasm and that lasts for about one full minute (Stahl, 2008), as reported by those who smoke heroin or use it intravenously. Other sensations reported by individuals who misuse heroin include a feeling of warmth under the skin, dry mouth, nausea, and a feeling of heaviness in the extremities. There is some degree of nasal congestion that develops, as heroin stimulates the release of histamine in the body. Individuals who misuse heroin also report a sensation of floating, or light sleep (“nodding off”) that lasts for about 2 hours, accompanied by clouded mental function. In contrast to alcohol, those who use heroin do not experience slurred speech, ataxia, or emotional lability while under the influence of heroin (Gutstein & Akil, 2006).

Other Opioids of Misuse

We will discuss some of the more commonly misused narcotic analgesics below.

CODEINE

Codeine has emerged as a drug of misuse, accounting for 10% of all drug-related deaths (Karch, 2009). There is little information available about codeine misuse, as this compound was long thought to be too weak to be of interest to individuals using drugs. It is possible that individuals who use heroin miscalculate the amount of codeine necessary to block opioid withdrawal symptoms, thus contributing to their deaths. However, this is only a theory, and the possibility of codeine being part of a fatal polydrug “cocktail” is always present.

OXYCONTIN

OxyContin® was released in 1995 and became a drug of misuse shortly afterward. A generic form of the substance oxycodone was introduced in 2004. Even before the generic form, it was estimated that 13.7 million persons in the United States had used OxyContin for nonmedical purposes in the year 2003 (Collins & Leak, 2008). Individuals intending to misuse this compound often crush the time-release spheres in the capsule and inject the material into a vein. Other individuals simply chew the tablets, defeating the time-release coating on the spheres, or take larger than prescribed doses for the euphoric effects.

OxyContin was heavily marketed by the company that introduced it, and only later was it revealed that they were quite aware of its misuse potential, but did not discuss this with prescribing physicians, but instead emphasized its supposedly low misuse potential (Meier, 2003).

It has been estimated that oxycodone alone is involved in approximately one-third of the estimated 12 million episodes of narcotic analgesic misuse each year in the United States (SAMHSA, 2016). Indeed, there is evidence that

the pharmacokinetics of this medication make it especially attractive to individuals intending to misuse drugs, which clouds the issue of whether it is a valuable drug in treating pain.

BUPRENORPHINE

In addition to its role as an opioid agonist treatment for opiate addiction, buprenorphine has emerged as a drug to misuse. It is well absorbed when administered sublingually, but bioavailability when swallowed is low since it is easily destroyed by digestive juices. Dosage levels are usually below 32 mg/day as there is little benefit to doses greater than this, and clinicians should be aware of the problem of drug diversion should the client request higher doses of this medication to block withdrawal symptoms. However, *intravenously* administered buprenorphine has a significant misuse potential. This practice is most common in Europe but has been verified as also occurring in the United States (Ling, Wesson, & Smith, 2005). It has been reported that this compound is misused either alone or in combination with diazepam, cyclizine, or temazepam. Unfortunately, because of buprenorphine's tendency to bind at the receptor site after activating it, naltrexone is of little use in a buprenorphine overdose since the latter medication works by blocking opioid receptor sites (Borg et al., 2014).

FENTANYL

Fentanyl has long been a popular drug to misuse because of its high potency, but it has recently gained worldwide attention (U.N. Office on Drugs and Crime, 2017). It is a prescription-only medication that is often diverted to the illicit drug market. Individuals have been known to smoke it, use it intranasally, or take transdermal patches, heat them, and inhale the fumes (Karch, 2009). Some individuals also take transdermal patches, poke holes in them, and consume the medication reservoir for use in any of the methods noted above, in addition to ingesting the liquid in the reservoir. Because of its high potency, it is easy to overdose on fentanyl, possibly with fatal results. It is often used to lace other drugs, including heroin, which has caused an increase in incidents of overdose (Bode, Singh, Andrews, Kapur, & Baez, 2017).

HYDROMORPHONE

Hydromorphone was introduced under the brand name of Dilaudid®, although it has since been introduced in a generic form as well. It is a chemical derivative of morphine but is about 8–10 times as powerful and is more lipid-soluble. This results in hydromorphone crossing the blood-brain barrier more rapidly than morphine, allowing for a more rapid onset of effects. Orally administered doses are poorly absorbed, and intravenous administration is the preferred route of administration. It is on occasion administered orally and is available in tablets that are in doses of 1–4 mg each. Peak blood levels

following oral administration are achieved in 30–60 minutes after ingestion. The half-life of this compound is estimated to be around 2.3 hours.

Individuals intending to misuse this substance often crush hydromorphone tablets and inject them, although the manufacturers do attempt to block this method of misuse by adding compounds to make this process very difficult or impossible. This is one of the reasons why oral hydromorphone is usually misused by injection. The side effects and risks associated with hydromorphone use are similar to those seen with morphine and will not be discussed again here. Hydromorphone has a high misuse potential and remains a popular drug among persons with an OUD.

PROPOXYPHENE

Propoxyphene is a compound that was sold under a number of brand names in the last quarter of the 20th century. This compound has little potential to induce euphoria by itself, but it was often used concurrently with methadone, providing a feeling of euphoria from the combined effects of these compounds. This compound has a significant misuse potential (Breggin, 2008); however, manufacture and use of this compound in the United States is now illegal.

While this list is not all-inclusive, it does underscore the misuse potential inherent in all prescription narcotic analgesics.

Methods of Opiate Misuse

When opiates are misused, the preferred method of misuse depends on the individual's experience with the compound. These compounds might be taken orally, injected under the skin ("skin popping"), administered intravenously, smoked, or used intranasally (technically, "insufflation"). The practice of smoking opium wastes a great deal of potential opium, and if supplies are limited (as they are in the United States), it is not a popular method of misuse.

Heroin, almost in a class of own, is misused in a variety of methods. The practice of insufflation and smoking heroin powder have become popular in the United States, fueled in part by the popular myth that you cannot become addicted to narcotics unless you *inject* drugs into your body (Drummer & Odell, 2001; Greydanus & Patel, 2005; Gwinnell & Adamec, 2006; Smith, 2001). When heroin is used intranasally, the method of administration is very similar to that seen when cocaine is used through insufflation. The individual will place the powder on a glass surface, then use a razor blade or knife edge to "dice" up the powder until it is a fine, talcum-like powder, which is arranged in a line on the glass and is then inhaled through a straw. In contrast to injected heroin, where the effects are felt almost instantly, it takes 10–15 minutes before inhaled heroin powder begins to

take effect. Injected heroin provides an intense rush, followed by a gentle sense of euphoria, which is the desired effect, and frequently a severe itching of the skin, nausea, and vomiting²⁹ (Gwinnell & Adamec, 2006).

Heroin is well absorbed through the lungs when it is smoked, although the onset of its effects is slower than when it is injected. The effects of heroin when it is smoked begins in 10–15 minutes, in contrast to the estimated 8 seconds before injected heroin begins to work (Gwinnell & Adamec, 2006). Smoking heroin is an ineffective method of delivery, with up to 80% of the available heroin being destroyed by the heat produced by the smoking process (Drummer & Odell, 2001). Drummer and Odell (2001) reported that when smoked heroin, blood levels are only about 50% as high as those seen when heroin is injected.³⁰ The practice of “chasing the dragon” is a variation on the process of smoking heroin. In this procedure, the individual heats some heroin powder on a piece of aluminum foil, using a cigarette lighter or match as the heat source. The resulting fumes are then inhaled, avoiding the exposure to intravenous needles that might be contaminated by other individuals (Karch, 2009). Another variation of the practice of smoking heroin is seen when individuals intermix heroin with crack cocaine pellets. This combination is said to enhance the high induced by these chemicals, although possibly at the cost of exacerbating the respiratory depression seen when narcotics are misused.

The most concentrated blood levels of heroin are achieved when the individual injects the compound into a vein. Sometimes the individual using heroin will mix “heroin in the spoon with water, or glucose and water, in order to dissolve it. Lemon juice, citric acid or vitamin C may be added to aid dissolving. This cocktail is heated until it boils, drawn into the syringe through a piece of cotton wool or cigarette filter to remove impurities, and injected whilst still warm” (Booth, 1996, p. 14). This method of misuse allows for the rapid introduction of concentrated heroin into the body, inducing an intense reaction, as noted elsewhere in this chapter. While veins in the arm are often used, some individuals will use arteries in the groin or the neck, on the theory that this will allow the heroin to more rapidly reach the brain.

Sources of Illicit Narcotics

Evidence would suggest that prescribed narcotic analgesics are the most commonly misused prescribed medication in New York City, and are more commonly misused

in that city than is heroin (Davis & Johnson, 2008). The authors found that the majority of the 586 participants in their study obtained medications from physicians. The authors discovered that methadone was the most commonly diverted substance, although other narcotic analgesics were also frequently diverted. The pharmaceuticals are obtained through a variety of channels. Sometimes the individual will “**make**” a doctor³¹ or dentist for a prescription, or will arrange for a person who receives medication for legitimate medical reasons to divert some of their medication. Some individuals who misuse opioids have been known to befriend a person with a terminal illness to steal narcotics from the person for their own use. Others have burglarized or brazenly held up pharmacies to demand narcotic analgesics. Pharmacies on the internet have become a major source of “prescribed” medications that are used for illicit purposes.

However, these sources cannot supply the individual with heroin, which is illegal in the United States. To meet the demand for heroin, an elaborate distribution network has evolved to smuggle heroin into the United States and distribute it across the country for sale to the individual. To avoid conflict over territory, upper-level distributors agreed that the heroin west of the Mississippi River would be smuggled through Mexico, while the heroin east of the Mississippi would be smuggled into the country from other sources. The heroin that is sold at the street level is usually adulterated³² with one or more foreign compounds, result being that the purity of heroin sold to individuals is around 47%, although occasionally one will find a sample that is up to 85% pure being sold on the street (O’Brien, 2008).

Although health care professionals have been known to divert pharmaceuticals for their own use, the strict controls over access and use of narcotic analgesics makes this increasingly difficult. Because they lack access to large amounts of their narcotic of choice, those who use illicit drugs will often attempt to inject a tablet or capsule originally intended for oral use. These oral administration vehicles contain compounds known as “**fillers**”³³ intended to give the capsule or tablet bulk, thus making it easier for the person to handle them. These compounds are not intended for intravenous injection, and normally are either destroyed by gastric juices or pass harmlessly through the gastrointestinal tract when ingested orally. The fillers or adulterants often mixed into illicit heroin potentially can form an embolus, or damage the vessel lining, and thus contribute to the formation of a blood clot at the site of injection. Repeated exposure to such compounds

²⁹Sometimes called “the good sick” by individuals who use heroin.

³⁰Individuals will compensate for the lower absorption level by smoking more heroin; this is why the two figures (amount destroyed when smoked versus blood levels) do not appear to make sense at first.

³¹See Glossary.

³²The topic of drug adulteration is discussed later in this text.

³³See Glossary.

can cause extensive scarring at the site of injection, forming the famous “tracks” associated with illicit opioid use.³⁴

The Development of Tolerance

The mechanism by which tolerance to a narcotic analgesic develops is poorly understood (Kreek, 2008; Reed et al., 2015). It is known that tolerance to a narcotic reflects the same biological process as neuroadaptation, but the former term is used when discussing drugs that are misused and the latter when discussing medications taken as prescribed. Tolerance to the effects of narcotics develops rapidly, often within days or weeks of continuous use. As is true for narcotic analgesics that are used as prescribed, tolerance does not develop to all of the drug’s effects. The individual using opioids illicitly can develop significant tolerance to the analgesic, respiratory, and sedating effects of opioids. They also become tolerant to the “rush” or “flash” effect that is initially experienced when they begin intravenously administered opioids (Jaffe & Strain, 2005). However, they still experience the narcotic-induced sense of gentle euphoria that is by itself an incentive for continued opioid use (Jaffe & Strain, 2005).

In spite of their growing tolerance to opioids, those misusing these substances never fully become tolerant to the meiotic and constipating effects induced by narcotic analgesics (Jaffe & Jaffe, 2004; Jaffe & Strain, 2005). Unfortunately, the chronic misuse of opioids may result in significant constipation problems for the individual, possibly to the point where s/he will form an intestinal blockage and require emergency surgery. Tolerance to the rush or flash develops rapidly, and individuals often attempt to compensate for this by either switching to a more effective delivery method (such as moving from intranasal to smoked forms of heroin), or by increasing the amount of drug consumed (O’Brien, 2001). These doses would be fatal to an opiate-naïve person, and it is not uncommon for individuals misusing opiates to miscalculate their level of tolerance and accidentally overdose. Approximately 50% of individuals misusing opioids will experience at least one drug overdose (Schuckit, 2008b, 2010b). Other individuals will go through cycles of drug use until their tolerance is such that they can no longer afford the necessary drugs to induce the desired state of euphoria, and then go through a period of withdrawal (usually with support from other illicit drugs, such as illicit benzodiazepines). Upon completion of the withdrawal cycle, they will restart the use of opiates again. Eventually, the individual reaches a point where s/he is no longer using drugs to achieve a high, but “just to maintain” the intoxicated state.

³⁴Which some individuals who use intravenous drugs might attempt to hide through the use of strategically placed tattoos (Greydanus & Patel, 2005).

Scope of the Problem of Opiate Misuse and Opiate Use Disorders

Physical dependence on opioids can develop in a very short time, possibly after just a few days of continuous use (Ivanov et al., 2006; Stahl, 2008). The United Nations estimated that there were 33 million opioid users worldwide. Of this number, 17.4 million use opium, morphine, or heroin (U.N. Office on Drugs and Crime, 2017). The misuse of opium is a localized phenomenon, however, and globally heroin misuse is much more common. In the United States, there has been a drastic increase in opioid misuse. As of 2015, 0.3 million people over the age of 12 had used heroin in the month prior to the survey and 4 million had misused prescription pain relievers in 2015 (SAMHSA, 2016). As of 2016, the use of heroin and prescription pain relievers increased, with 11.5 million individuals misusing prescription pain relievers in 2016 and close to 0.5 million with past-month heroin use (SAMHSA, 2017).

It has been estimated that between one-quarter and one-third of those who *briefly* abuse opiates go on to become addicted to one of these compounds (O’Brien, 2006; Sommer, 2005).³⁵ The development of an addiction to narcotics usually requires a period of increasingly frequent misuse; however, some individuals report that they became addicted to a narcotic after using it just once. There is thus significant variability among individuals as to how long it takes before an addiction to narcotics develops. Males tend to dominate the opioid addiction problem by a ratio of about 3:1 (Sadock, Sadock, & Ruiz, 2015). Using the estimate of 2.6 million persons with an opioid use disorder in the United States (SAMHSA, 2016), this would mean that approximately 1.95 million are male, and 650,000 are female.

In contrast to those who report becoming addicted to a narcotic after using it just one time, there is a curious subpopulation of individuals known as “chippers.” The chipper might misuse opioids in response to social cues, but will have no trouble abstaining from narcotics when they wish to do so; they do not experience craving for narcotics in between periods of active use, and can refuse invitations to misuse narcotics if they are not interested in doing so. However, very little is known about opioid chippers, who have not been the subject of much research. Some of those who once were classified as chippers go on to become addicted, some discontinue the use of these compounds after a period of experimental use, while still others remain chippers.

PRESCRIPTION NARCOTIC DIVERSION

The diversion of prescribed analgesics has emerged as a significant part of the narcotic use disorder problem in the United States, reflecting the 400% increase in the number

³⁵However, since it is not possible to identify who will become addicted, the abuse of narcotic analgesics is not recommended.

of prescriptions for a narcotic analgesic in the country during the 1999–2015 time span (Murphy, 2012), providing an ever-growing number of prescriptions that might be diverted to the illicit drug market. Researchers have discovered that 76% of those narcotic analgesics that are misused were prescribed for somebody other than the individual using them, 20% were prescribed to the individual using them but either the need for these medications no longer existed or they were being used at higher doses than prescribed, and the remainder came from other sources (Miller & Frankowski, 2012). Death from diverted narcotic analgesics, especially among those inexperienced in opiate use, is a major problem in the United States. In contrast to the 3,036 deaths attributed to heroin overdoses in the country in 2010, 16,651 individuals died of an overdose of prescription narcotic analgesics in that same time period (Volkow, Frieden, Hyde, & Cha, 2014). The number of people who die from heroin overdoses has slowly been increasing each year, possibly as a response to growing restrictions on pharmaceutical narcotics forcing opiate-dependent people to switch to heroin as an alternative.

It is not uncommon for some persons misusing opiates to visit different physicians or hospital emergency rooms to obtain multiple prescriptions for the same medication(s). Such individuals will often study medical textbooks to be able to simulate symptoms of a disorder virtually guaranteed to provide them with a prescription for a narcotic analgesic. Some individuals have even been known to have a tattoo that simulates the scar of a surgical procedure, especially a back surgery, to justify a prescription for narcotic analgesics from a new physician. If stopped by the police, they are able to produce a prescription bottle with their name on it, affirming that there is a “legitimate” need to use the medication.

SCOPE OF ILLICIT HEROIN MISUSE IN THE UNITED STATES

Heroin is the prototypical narcotic that the public thinks of when they hear the term “opioid use disorder.” Even in the world of heroin misuse, there are subdivisions that further complicate the clinical picture of heroin use disorders in the United States: There are those who *misuse* heroin on an infrequent basis and who never progress to a heroin use disorder (chippers). Some of this subgroup start by “chipping” heroin, but find that it becomes increasingly important to their daily living and develop an opioid use disorder. Those persons with an opioid use disorder are broken down into three subgroups: (a) persons in the process of developing an active heroin addiction, (b) those who are still actively addicted to this compound, (c) either participating in an opioid agonist treatment program or (d) abstaining from opioid use on their own. Over half a million individuals met criteria for a heroin use disorder in 2015, 10% of the estimated 5 million people in the United States who have used heroin

at least once (SAMHSA, 2016). Heroin addiction does not develop instantly, but will usually require approximately 2 years between the initiation of heroin use and the time that the individual has become physically dependent on it.

Heroin is cheaper than prescription analgesics such as OxyContin, and individuals tend to be Caucasian, middle-class, and in their mid-twenties when they first use heroin. Women are about as likely to use heroin as men at this time. Individuals often switch from the more expensive prescription narcotics obtained through illicit channels to heroin to be able to afford their growing need for narcotics. As this data suggests, prescription narcotic misuse in the United States often serves as a “gateway” drug for the misuse of and possible eventual addiction to heroin.

Complications Induced by Opiate Misuse or Opiate Use Disorder

The complications seen in individuals who misuse opiates on a chronic basis fall into two categories: (1) those that are exaggerations of the complications seen when these compounds are seen in medical practice, and (2) those that are forced on the individual by the lifestyle built around the need for opiates. Persons with an opiate use disorder face a significant threat of premature death, the most common causes of which are accidental overdose and cardiopulmonary failure (Fiellin, 2008; Smyth, Hoffman, Fan, & Hser, 2007). There are approximately 18,898 opiate-related deaths in the United States each year (Rudd, Aleshire, Zibbell, & Gladden, 2016). Opiate-related deaths can occur at any point in the individual’s opiate use career. Smyth and colleagues (2007) found, for example, that of their original participant pool of 581 individuals with severe OUD admitted to treatment in California, after 33 years 48.5% of the original sample pool had died. The leading causes of death were overdose (17% of those who had died), chronic liver disease (15%), cardiovascular disorders (12%), cancer (11%), accidents (8%), and homicide (7%). The typical individual addicted to heroin is thought to lose approximately 18.3 years³⁶ of potential life either directly or indirectly as a result of their addiction (Smyth et al., 2007; Tomb, 2004). Other potential causes of death include cerebral infarction and the formation of a thrombosis that can result in a stroke (Ricaurte, Langston, & McCann, 2008). Occasionally, individuals misusing these substances will develop aspiration pneumonia because of drug-induced respiratory suppression

³⁶ If you assume that the average addict would have lived 80 years if he or she were not addicted to heroin, this means that the typical heroin addict loses about 22% of his or her estimated life because of their addiction to heroin.

(Schuckit, 2010b). This condition, like all forms of pneumonia, carries with it the risk of premature death.

NARCOTIC WITHDRAWAL SYNDROME

The narcotic withdrawal syndrome experienced by those who misuse opiates is simply the opioid discontinuance syndrome observed when persons use narcotic analgesics under a physician's supervision. The narcotic withdrawal syndrome is possibly more intense than the discontinuance syndrome seen in normal medical practice because of the use of higher doses of opiates for longer periods of time than is the norm in medical practice. It should be noted, however, that in spite of common claims by those who misuse opioids, the narcotic withdrawal syndrome is only rarely a life-threatening condition³⁷ (Fadem, 2009; Maldonado, 2010; Virani, Bezchlibnyk-Butler, & Jeffries, 2009). In reality, withdrawal distress has been compared to a severe case of influenza (Hari, 2015; Kosten & O'Connor, 2003; Tomb, 2008). There are two stages to the opioid withdrawal syndrome: (a) the stage of *acute* withdrawal and (b) the stage of *extended* withdrawal. Both of these stages are influenced by such factors as (1) the specific compound(s) being misused,³⁸ (2) the length of time that these compounds have been used, (3) the speed at which the withdrawal progresses, and (4) the individual's cognitive "set" (Jaffe & Jaffe, 2004; Kosten & O'Connor, 2003). Health care professionals might use the Clinical Institute Narcotics Assessment (CINA) to obtain an objective assessment tool for the withdrawal process (Mee-Lee & Gastfriend, 2008).

Obviously, the specific compound being used will influence the withdrawal process. Acute heroin withdrawal symptoms, for example, peak 36–72 hours after the individual's last dose, and last for 7–10 days. In contrast to this, the acute withdrawal symptoms from methadone peak 4–6 days after the last dose, and continue for 14–21 days (Collins & Kleber, 2004; Kosten & O'Connor, 2003; Kreek, 2008). The withdrawal patterns for other opioids are similar, although there might be some variation depending on the half-life of the compound(s). The speed of the opioid withdrawal process is another factor that influences the symptoms experienced, and their duration. A person with a tolerance to opiates who is placed on a methadone "taper" will experience withdrawal symptoms over prolonged periods of time as his/her medication is slowly reduced. However, these withdrawal symptoms will be less intense than if the person just stopped misusing drugs ("cold turkey"). The individual's withdrawal distress

would be of shorter duration in the latter case. Thus, physicians must balance the individual's discomfort with the speed of the withdrawal process.

The individual's cognitive "set" also influences the withdrawal process and the individual's perception of it. This reflects such factors as the individual's knowledge, attention, motivation, and degree of suggestibility. The influence of the individual's cognitive set might be seen in extreme cases such as when the individual develops an almost phobic fear of withdrawal (Collins & Kleber, 2004; Kenny, Chen, Kitamura, Marku, & Koob, 2006). Such individuals might have no personal investment in the success of the withdrawal process and thus are motivated to respond to every symptom as if it were major trauma being inflicted on them. In contrast to this, the highly motivated client might be eased through the withdrawal process through hypnotic suggestion (Erllich, 2001).

During the acute phase of opioid withdrawal, the individual usually reports an intense craving for more narcotics and will experience such problems as tearing of the eyes, runny nose, repeated yawning,³⁹ sweating, restless sleep, dilated pupils, anxiety, anorexia, irritability, insomnia, weakness, abdominal pain, nausea, vomiting, gastrointestinal upset, chills, diarrhea, muscle spasms, and in males possible ejaculation (Brust, 2004; Collins & Kleber, 2004; Gunderson & Stimmel, 2004; Kreek, 2008). During the period of acute withdrawal, the individual might report feeling more sensitive to pain as a result of increased muscle activity and the stimulation of the sympathetic nervous system (Gunderson & Stimmel, 2004; Kreek, 2008).⁴⁰ It has been suggested that 600–800 mg of ibuprofen every 4–6 hours can provide significant relief from the muscle pain experienced by many persons during this phase of withdrawal (Collins & Kleber, 2004). Withdrawal-related anxiety might be so intense as to serve as a relapse trigger (Collins & Kleber, 2004). However, rather than using a benzodiazepine, the compound Seroquel® (quetiapine fumarate) has been recommended to control withdrawal-induced anxiety (Winegarden, 2001).

On very rare occasions, the opioid withdrawal process can cause seizures or exacerbate a preexisting seizure disorder (Collins & Kleber, 2004; Gutstein & Akil, 2006; Kreek, 2008). The narcotic meperidine is especially well known to lower the individual's seizure threshold and is rarely prescribed for this reason. It is also important to make sure that

³⁷Usually, life-threatening withdrawal is seen in persons with concurrent medical problems. All cases of drug withdrawal should be assessed and treated by a physician to ensure proper medical care during this process.

³⁸Including the half-life of each compound.

³⁹A process which, according to Newberg and Walkman (2009), reflects the brain's efforts to "reset" the cognitive pathways so that they can adjust to the change in neurotransmitter levels within the opioid neurotransmitter system.

⁴⁰A medical examination will reveal whether the reported withdrawal distress is caused or exacerbated by a concurrent medical condition that needs treatment (Gunderson & Stimmel, 2004).

patients with a known seizure disorder have been compliant with anti-epileptic medications to avoid having the withdrawal process exacerbate their seizure disorder.

EXTENDED OPIOID WITHDRAWAL SYMPTOMS

The phase of extended opiate withdrawal might last for several months in some individuals and will include symptoms such as fatigue, heart palpitations, “urges” to return to opioid use, and a general feeling of restlessness (Jaffe & Strain, 2006). Some persons also report concentration problems that might last 3–6 months after their last use of narcotics. These feelings become less intense over time, and the individual’s level of function returns to normal over a period of weeks to months.

A CAUTIONARY NOTE

Many individuals will emphasize their physical distress during the withdrawal process in the hopes of obtaining drugs to limit their distress and possibly provide a substitute for the unavailable opioid. Such displays are often quite dramatic, but are hardly realistic for the most part. Mild to moderate opioid withdrawal is, while uncomfortable, rarely a medical emergency in the healthy adult⁴¹ (Baron et al., 2009). The subjective experience has been compared to a bad case of influenza, and will abate in the healthy individual even without medical intervention.

ORGAN DAMAGE

Some persons who experience extreme pain, such as that seen in some forms of cancer, for example, receive massive doses of narcotic analgesics for extended periods of time without any sign of drug-induced organ damage (Ricaurte et al., 2008). However, these are cases where the person is using pharmaceutical-quality narcotic analgesics, and not the “street” drugs commonly used by those seeking to misuse these substances. These compounds are of questionable purity, and are usually intermixed with compounds not intended for injection. There is little data on the health consequences of the misuse of other opioids beyond heroin.

Common health complications seen in those who misuse heroin include strokes, cerebral vasospasm, infectious endocarditis, botulism, tetanus, peptic ulcer disease, liver failure, disorders of the body’s ability to form blood clots, malignant hypertension, neuropathy, pulmonary edema, and uremia⁴² (Brust, 2004; Greydanus & Patel, 2005; Karch, 2009). The

misuse of illicit narcotics has also been found to reduce the effectiveness of the immune system, although again the exact mechanism for this disorder is not understood at this time (Karch, 2009). Individuals who misuse intravenous opioids are at increased risk for rhabdomyolysis, but it is not clear whether this is because of the effects of the narcotics, or of one or more adulterants mixed with the illicit narcotics (Karch, 2009). Individuals who misuse oxycodone appear to be vulnerable to developing an autoimmune disorder that attacks the kidneys, although the causal mechanism is again unknown (Hill, Dwyer, Kay, & Murphy, 2002).

The recreational misuse of opioids appears to induce the shrinkage of the brain’s reward system. This appears to reflect an adaptive response by the brain to the constant presence of an opioid such as heroin, and may reflect the biological basis for tolerance to the euphoric effects of such compounds. With extended abstinence, this effect appears to reverse itself. The practice of smoking heroin has been identified as causing a progressive spongiform leukoencephalopathy⁴³ in rare cases (Zevin & Benowitz, 2007). It is not known whether this effect is induced by the heroin itself or by one of the adulterants mixed into the illicit heroin before sale (Ropper & Brown, 2005; Schuckit, 2008b). There was an outbreak of heroin-induced progressive spongiform leukoencephalopathy in the Netherlands in the 1990s, a condition that is rarely encountered in the United States, but which has debilitating consequences for the victim. Intravenous opioid misuse has also been seen to induce damage to peripheral nerves as the individual rests for extended periods of time in the same position, cutting off the blood flow to the affected nerves. Also, nerves near the injection site might be damaged by the adulterants mixed with the illicit drug being injected (Ropper & Brown, 2005).

COTTON FEVER

As noted earlier, individuals will attempt to “purify” the heroin about to be injected by pouring it through wads of cotton or cigarette filters. During times of hardship, some individuals will attempt to use the residual heroin found in these filters, and, in the process, will inject microscopic cotton particles as well as the impurities that had originally been filtered out. This will induce a condition known as **pulmonary arteritis**⁴⁴ (which is called “cotton fever” by those who use heroin).

MATURING OUT OF NARCOTICS MISUSE

A curious phenomenon that has been observed is that heroin use appears to taper off in the 39+ age cohorts (Hari, 2015). This appears to be independent of those individuals

⁴¹Assuming that the individual was misusing only narcotics, and that s/he has not overdosed on an opioid or combination of drugs. The latter situation is a medical emergency that requires immediate intervention by a trained medical team (O’Brien, 2001; Sadock et al., 2015; Work Group on Substance Use Disorders, 2007; Zevin & Benowitz, 2007).

⁴²Many of these complications are a result of the lifestyle forced upon the typical person with a heroin use disorder, or by the adulterants added to illicit heroin, and not by the heroin itself.

⁴³Similar to “mad cow” disease.

⁴⁴See Glossary.

who are not able to misuse narcotics because of death or incarceration, and substance rehabilitation counselors often hear persons addicted to narcotics admit that they no longer feel a sensation of euphoria when they inject the drug, but that they just go through the motions because it has been a ritual in their lives for so long. Obviously, there is a need for more research into this phenomenon, its biochemical basis, and whether any useful pharmaceutical interventions could be developed to assist opiate-dependent persons to abstain from narcotics more easily.

Overdose of Illicit Narcotics

Ropper and Brown (2005) identified of four mechanisms through which the individual using opiates might overdose: (a) a suicide attempt, (b) the use of substitute or contaminated illicit drugs, (c) an individual's unusual sensitivity to the drug(s) being used, and (d) errors in calculating the proper dosage. It has been estimated that at least 50% of those who use illicit heroin will overdose at least once, possibly with fatal results. Indeed, death may result so quickly that the individual is found with the needle still in his or her arm. The current theory is that that death is the result of respiratory depression (Gutstein & Akil, 2006). An unknown but significant number of persons overdose on prescription narcotic analgesics diverted to the illicit drug market as well (Dunn et al., 2010; Webster et al., 2011). Research indicates at least a doubling of increased risk of suicide, up to 13 times greater risk in those diagnosed with opioid use disorders, in both men and women, with greater risk seen in men (Ashrafioun, Bishop, Conner, & Pigeon, 2017; Bohnert, Ilgen, Louzon, McCarthy, & Katz, 2017; Wilcox, Conner, & Caine, 2004).

Some of the symptoms of an opioid overdose include reduced level of consciousness, pinpoint pupils, cerebral edema, and respiratory depression (Drummer & Odell, 2001; Schuckit, 2006a). Even if the individual should survive the overdose, there might be residual effects such as partial paralysis, blindness, or peripheral neuropathies induced by the overdose (Dilts & Dilts, 2005). The onset of specific overdose symptoms is dependent on the compound(s) ingested or injected. For example, if methadone were the compound ingested, the first symptoms might not manifest for up to 3.2 hours after the overdose, and respiratory depression might require up to 8 hours to begin to appear (LoVecchio et al., 2007). To further complicate matters, the practice of using multiple illicit drugs with the potential additive effects of various adulterants in the compound(s) being used often clouds the clinical presentation of an overdose. For example, there is evidence that the concurrent use of marijuana and heroin might increase the individual's risk of a narcotics overdose through an unknown mechanism (Drummer & Odell,

2001). The practice of using amphetamines or cocaine might hide the symptoms of the overdose until it is too late to seek medical attention, since the stimulants might mask the early symptoms of an opioid overdose.

Even in the best-equipped hospital, an opioid overdose can be fatal. The current treatment of choice for an opioid overdose is a combination of respiratory and cardiac support and the intravenous administration of Narcan® (naloxone hydrochloride) (Ropper & Brown, 2005). This compound binds at the opioid receptor sites, blocking the opioid molecules from reaching them. If administered in time, this will reverse the narcotics overdose. However, the therapeutic half-life of Narcan is only 60–90 minutes, and several doses might be necessary before the person fully recovers from the overdose. In the case of long-acting narcotic analgesics such as methadone, the individual might require Narcan infusions for days to avoid long-term overdose effects. There is the additional danger of side effects of naloxone hydrochloride. These side effects will need to be assessed by the attending physician, and if severe enough to warrant intervention will need to be addressed by the attending health care professionals as well.

Opioid Use or Misuse and the *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) identified five subforms of opioid-related disorders:

- Opioid use disorder
- Opioid intoxication
- Opioid withdrawal
- Other opioid-induced disorders
- Unspecified opioid-related disorders

Opioid use disorder (OUD) as defined by the DSM-5 is equivalent to addiction to narcotics, as discussed in this chapter. The DSM-5 definition of opioid use disorder identifies criteria that might indicate OUD, including tolerance and opiate withdrawal. The presence of any two of the diagnostic criteria within a 12-month period is evidence of an OUD, except when the individual is taking a narcotic analgesic as prescribed, according to the DSM-5. The DSM-5 definition of OUD also allows for the use of four modifiers:

1. in early remission,
2. in sustained remission (although craving for opioid use is exempt from the criteria for remission),
3. on opioid maintenance therapy, and
4. in a controlled environment.

Opioid intoxication is defined in the *DSM-5* as reflecting the recent use of an opioid, inducing symptoms such as drowsiness or coma, slurred speech, or memory impairment/attention impairment, none of which can be attributable to another condition. It is noted that rarely does the individual experience “perceptual disturbances” (*American Psychiatric Association, 2013, p. 546*) that again cannot be attributable to another medical condition. The use of sedating drugs such as barbiturates or benzodiazepines can induce symptoms very similar to those seen in opioid intoxication, and the probable use of these compounds must be eliminated before an individual is diagnosed with opioid intoxication (*American Psychiatric Association, 2013*).

The *DSM-5* classification of *opioid withdrawal* is essentially the same as identified in this text. There is, however, the warning that the apparent opioid withdrawal symptoms do not reflect withdrawal from another substance, or a medical condition capable of inducing withdrawal-like symptoms. The category of *other opioid-induced* disorders refers to conditions such as depression, which can be a consequence of opioid misuse or withdrawal. If the individual were to have clinically significant distress, but not meet criteria of any of the other relevant diagnostic categories, this would be classified as *unspecified opioid-related disorders* in the *DSM-5* (*American Psychiatric Association, 2013*).

Chapter Summary

The opioids have been effectively used for thousands of years to treat pain. After alcohol, one could argue that opium is one of the oldest drugs used by humans, with a known history going back thousands of years prior to the invention of writing. With the onset of the chemical revolution of the 18th and 19th centuries, chemists began to isolate the active compounds found in opium, producing a family of compounds that were found to be useful in controlling severe pain, severe cough, and severe diarrhea. It was soon discovered that the compounds isolated from opium, and their chemical cousins, presented the user with a significant misuse potential, as well as the potential for addiction.

With the advent of semisynthetic and synthetic opioids, chemists attempted to find a compound that would retain the analgesic potential of morphine, which has emerged as the gold standard for analgesia. There is an ongoing search for an effective analgesic for severe pain without the negative effects associated with the use of opioids. Unfortunately, this search has failed to yield such a compound yet, although it has provided a wide range of narcotic analgesics which have the potential to be misused and induce addiction. These compounds have become the subject of great controversy both in the field of medicine and among members of the general public.



CHAPTER 12

Hallucinogen Misuse

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 12.1** Understand the history of hallucinogens
- 12.2** Understand the scope of the problem of hallucinogen misuse
- 12.3** Comprehend the pharmacology, methods of use, and subjective effects of hallucinogens
- 12.4** Describe the complications of hallucinogen use
- 12.5** Understand the *DSM* criteria for hallucinogen-related disorders

Introduction

To older persons, the term “hallucinogen” is associated with the “Summer of Love”¹ in San Francisco, when arguably the hallucinogenic compounds that fueled the “psychedelic” craze reached their pinnacle (Traub, 2009). In the time since then, these compounds have waxed and waned in popularity as drugs of misuse, although technically they have been classified as illegal substances with no known medicinal value. While they are perhaps less commonly used now than in past decades, hallucinogenic compounds are still occasionally sought out by those who use illicit drugs. Other individuals who misuse substances are unwittingly exposed to a hallucinogen that was used to bolster the apparent effect of low-quality marijuana or sold under the guise of another compound. As will be discussed in Chapter 37, in the world of illicit drugs it is a case of “let the buyer beware.”

Scientists have concluded that there are hundreds of different species of plants that contain compounds that might, if smoked or ingested, alter the user’s state of consciousness. Although it is rarely thought of in this light, the tobacco plant is one such plant.² Some of the hallucinogenic compounds have been used in religious ceremonies, healing rituals, and for predicting the future (MacLean, Johnson, & Griffiths, 2015; Metzner, 2005; Sessa, 2005; Traub, 2009).

¹The summer of 1967, for those who are just a little too young to remember this year from personal experience.

²Discussed in Chapter 15.

One example is peyote, which anthropologists believe has been used for its hallucinogenic effects for at least 4,000 years (Nichols, 2006; Traub, 2009). The advent of the chemical revolution in the late 19th and 20th centuries saw many of these natural compounds isolated and a range of synthetic hallucinogenic compounds developed in various laboratories around the world.

In the United States, certain religious groups continue to use mushrooms that contain the hallucinogenic psilocybin. Scientists in this country who for the most part have long shunned research on the hallucinogens³ are now actively investigating whether at least some of the known hallucinogenic compounds might have medicinal value (Brown, 2007; Jacobsen, 2014; Karch, 2009; Ross, 2012). LSD is being considered as a possible aid in the treatment of alcoholism (Krebs & Johansen, 2012) and anxiety (Gasser, Kirchner, & Passie, 2015), while MDMA is being investigated as a possible treatment aid in the treatment of posttraumatic stress disorder and anxiety (Sessa, 2017), and ketamine as a possible aid in the treatment of depression (Mathew & Zarate, 2016) as well as severe agitation (Riddell, Tran, Bengiamin, Hendey, & Armenian, 2017). Psilocybin is being investigated as a possible aid in the treatment of obsessive compulsive disorder (Daniel & Haberman, 2017). Recent research indicates the possible use of psilocybin to help terminally ill patients face the reality of their impending death, the individual's anxiety, and the existential issues raised by their illness (Griffiths et al., 2016; Ross et al., 2016; Weir, 2015). Although the drug experience is poorly understood and there are reports of negative outcomes, for the most part, therapists report significant improvement in the individual's mood and a reduction in their anxiety levels after psilocybin therapy, often after a single session (Weir, 2015). However, as of this time, psilocybin remains a prohibited substance and there are no medical applications for this compound recognized by the Drug Enforcement Administration, which maintains its usual stance of inhibiting research into possible medicinal properties of a substance in these compounds even as there is a need for more research into such medical applications (Jacobson, 2014).

³Aided in part by the classification of these compounds as Category I compounds as defined by the Comprehensive Drug Abuse Prevention and Control Act of 1970, a step that made even legitimate experimental use of these compounds illegal.

In spite of their legal status for civilians, the U.S. government has long held an interest in these compounds. The U.S. Army, for example, looked at LSD (discussed below) as a possible chemical warfare agent, going so far as to administer the compound to soldiers without their knowledge or consent (Talty, 2003). The Central Intelligence Agency (CIA) is known to have experimented with some of the hallucinogen as possible agents to aid interrogation. In the middle of the 20th century, some individuals advocated their use as a way to explore alternative realities, or to gain self-knowledge, trends that have continued (Metzner, 2002). The majority of hallucinogens were classified as Category I compounds by the Comprehensive Drug Abuse Prevention and Control Act of 1970, and overnight were transformed into illegal substances. In this chapter, some of the most popular hallucinogenic compounds will be discussed.⁴

A Short History of Hallucinogens

Over the years, chemists have isolated and studied approximately 100 different hallucinogenic compounds that are found in various plants or mushrooms.⁵ Psilocybin is an example of one such compound. Psilocybin is found in certain mushrooms indigenous to the southwestern United States and northern Mexico. However, there are a large number of other natural hallucinogenic compounds that have never been isolated or studied by scientists, and there is the possibility that additional hallucinogenic compounds will continue to be isolated (Glennon, 2004; Smith & Morely, 2017). Experimental pharmacologists have also developed synthetic compounds with hallucinogenic effects, one of which is phencyclidine (PCP),⁶ which became a part of the drug misuse problem in the United States since shortly after it was developed.

One family of compounds that has been subjected to intense scientific scrutiny are those chemicals produced by the ergot fungus, which grows on various forms of grain.

⁴On occasion a person will use venom from the species of toad known as *Bofu gargarizans* to induce hallucinations. There is a very narrow margin of safety for this toxin and users find that it is easy to reach a lethal dose in their quest for a hallucinogenic dose. Because of its toxicity and the fact that it is rarely encountered in the United States, it will not be discussed again.

⁵Although at first glance this statement might seem to be in conflict with the statement in the introduction that "thousands" of plant species contain hallucinogenic compounds, it is important to keep in mind that the same compound might be found in a number of different plants.

⁶Discussed later in this chapter.

Some compounds produced by this fungus have been found to induce such severe vasoconstriction that an entire limb has been known to **auto-amputate**⁷ or cause the individual to die of gangrene (Walton, 2002). Historians believe that ergot fungus induced a widespread illness in the Aquitaine region of France around the year 1000 B.C.E.,⁸ causing the death of at least 40,000 people who consumed bread made from contaminated grain (Walton, 2002).

Because these compounds were so potent, scientists tried to isolate them to explore potential medicinal uses. In 1943, during a clinical research project exploring the possible application of a compound obtained from the rye ergot fungus *Claviceps purpurea* to find a compound that might be used to treat headaches, one of the chemists, Albert Hoffman, accidentally inhaled or ingested a microscopic amount of a compound produced by the strain of fungus under investigation. He began to experience hallucinations and visual perceptual distortions, which he correctly attributed to a compound produced by the strain of *Claviceps purpurea*. The next day, after recovering from the effects of the first unintentional exposure, he ingested a small amount of the fungus, and again experienced the same effects. His experiences sparked research to isolate the compound responsible for these effects, eventually yielding lysergic acid diethylamide-25 (LSD-25, or simply LSD) as the causal agent.

Following World War II, there was a great deal of scientific interest in the effects of various hallucinogens, sparked in part by the similarities between their effects and the symptoms of various forms of mental illness. In the 1950s, scientists coined the terms *psychedelics* or *hallucinogenics* to identify this class of compounds. They were the focus of both scientific investigation because of their ability to induce hallucinations in a manner similar to those of schizophrenia, and research by the military as possible weapons of war. The unethical nature of the latter investigations is clearly demonstrated by the army's administration of LSD to unsuspecting recruits in the 1960s to observe its effects on the soldiers (O'Meara, 2009). Such a potent compound also became the focus of informal experiments by those who misused drugs in the 1960s and early 1970s as a way to liberate the mind from the shackles of conventional thought. The most popular of these compounds, LSD and later phencyclidine (PCP), were classified as Schedule I controlled substances in 1970 by the Drug Enforcement Administration.⁹ However, this did not prevent these compounds from becoming popular drugs of misuse in the last four decades of the 20th century,

and, as noted in the "Introduction," hallucinogens are often sold as other substances or occasionally intentionally used by those seeking their effects.

Scope of the Problem

The misuse of hallucinogens in the United States involves a minority of adolescents and young adults for the most part. Nationally, 15.3% of persons over the age of 12 are thought to have used a hallucinogen at some point in their lifetime, with 9.5% using LSD, 2.4% indicating phencyclidine (PCP), and 6.8% had used MDMA (SAMHSA, 2016). However, these figures reflect lifetime *prevalence*. In the preceding year, 0.6% of individuals were thought to have used LSD, less than 0.05% used PCP, and 1% are thought to have used MDMA (SAMHSA, 2016).

For the greatest proportion of individuals who take hallucinogens, their use of these compounds reflects transient, possibly experimental use. This conclusion is supported by the observation that in contrast to the number of people who have used MDMA, noted above, only about 0.2% are monthly users of MDMA in this country (SAMHSA, 2016). This data is consistent with the observation that while the hallucinogens are less popular than in past generations, they are still used. An exception to the general decline in hallucinogen use is *Salvia divinorum*, a compound that has recently exploded onto the drug scene in the United States. It is thought that 1.9% of individuals over the age of 12 have used this substance (SAMHSA, 2016). Again, the data suggests that the greater proportion of these people tried this compound out of curiosity.

Pharmacology of the Hallucinogens

The effects of these compounds have not been studied in depth (Glennon, 2008), and the overall understanding is based on testing on animals (Halberstadt & Geyer, 2017). It is believed that the effects of a hallucinogen are based on factors such as (a) the dose administered, (b) the specific compound used, and (c) the route of administration (Weiss, 2007). Hallucinogens are thought to alter the delicate balance of neurotransmitters in the brain, especially the Serotonin 2a receptor site, thus producing their effects.¹⁰ The dopamine neurotransmitter system is also affected by

⁷See Glossary.

⁸Or, *before the common era*. This term replaces the older term *A.D.*

⁹See Appendix 3.

¹⁰The truth of this statement is easily supported by the experience of persons who suffer from a high fever during illness, or diabetic patients whose blood sugar levels fall to dangerously low levels. Each group of patients reports distorted perceptions of reality, and behave in abnormal ways.

the hallucinogens. Although compounds such as dopamine and serotonin are viewed as neurotransmitters they might also be viewed as *neuromodulators*, shifting the activity of neurons from one state to another. Subjectively, the experience of these neural activity shifts is reflected in such activities as concentration on a specific task, the euphoria experienced in a new love relationship, or the amnesia of sleep (Hobson, 2001). Disorders of this neurological balance during waking would then cause various abnormal brain states, such as those induced by the hallucinogens (Hobson, 2001). By altering the balance of neurotransmitters in the brain, it is possible to change the individual's subjective experience of consciousness.

The classic hallucinogens are often divided into two major groups (MacLean et al., 2015): (1) the phenethylamines (mescaline and MDMA fall into this class of compounds), which have a core structure similar to that of the neurotransmitter norepinephrine, and (2) the tryptamines (which includes, among other compounds, both psilocybin and DMT), which have a core structure similar to the neurotransmitter serotonin. Some authors divide hallucinogens into slightly different categories: psychedelics (such as mescaline, psilocybin, and DMT), enactogens (such as NMDA and MDMA), and dissociative anesthetics (such as DXM and ketamine) (Garcia-Romeu, Kersgaard, & Addy, 2016). There are also atypical hallucinogens, which include ibogaine, as well as salvinorin A (Garcia-Romeu et al., 2016). The mechanism through which the hallucinogens alter the normal balance of neurotransmitters is still being explored. Research evidence, for example, would suggest that LSD, like most of the other hallucinogenic compounds, acts as an agonist to the 5-HT serotonin receptor site, and the effects of this compound are blocked by experimental 5-HT serotonin receptor site antagonists (Drummer & Odell, 2001; Glennon, 2004; Halberstadt & Geyer, 2017).

In spite of their classification as *hallucinogens*, these compounds do not produce frank hallucinations except at very high doses¹¹ (Jones, 2005; O'Brien, 2011). At the doses normally used by individuals in the United States, these compounds reduce perceptual distortions (Jones, 2005; Tacke & Ebert, 2005). On a cellular level, neurons that normally fired together lost synchronization, which is experienced as a disintegration of the individual's sense of self, or ego. Individuals using these substances adjust their intake of the compound to produce just the effects that they desire, usually perceptual distortions (Schuckit, 2006a). It is common for the individual using hallucinogens to believe that s/he has achieved a new insight into reality while under the influence of one

of these substances. These perceptions do not usually prove to be of value, and for the most part are recognized by the individual as being drug-induced. Since LSD is the prototypical hallucinogen, and has been best studied, this chapter will focus on LSD first, and will focus on other compounds only as needed.

Methods of Misuse

Hallucinogens might be ingested orally, smoked, snorted, or injected, although the latter method of use is rather rare (MacLean et al., 2015; Mendelson & Mello, 2010; Weaver & Schnoll, 2008). The exact method of use depends on the specific compound. For example, LSD is usually ingested orally, while PCP (discussed later in this chapter) can be ingested orally, injected, or smoked. MDMA is usually ingested orally, although it might also be injected or inhaled (Klein & Kramer, 2004; Tacke & Ebert, 2005). Though the most common method of administration for LSD is ingestion, it can be administered intravenously or by inhalation. Casual users might find that a dose of 50 micrograms will cause perceptual distortions, although the classic LSD "trip" usually requires at least twice that dose. The potency of current illicit LSD samples is usually lower than those sold in the 1960s and 1970s, possibly to make the effects less frightening and more acceptable to the first-time user. Experienced individuals will thus use two or three typical doses to achieve the desired effects. Because the effects are so variable from one time to the next, Zuckerman (2012) suggested that individuals who usually use opioids tend to avoid LSD use.

The Pharmacology of LSD

LSD has been the subject of intense scientific scrutiny since it was first isolated; however, there is still a great deal to learn about how this compound affects the brain (Sadock, Sadock, & Ruiz, 2015). It is classified as a Schedule I¹² and as such is not thought to have medicinal value, although some researchers believe that it is a possible adjunct to the treatment of alcoholism (Krebs & Johansen, 2012; Ross, 2012) and anxiety (Gasser et al., 2015). It has been estimated that LSD is between 100 and 1,000 times as potent as natural hallucinogens such as psilocybin and peyote, and perhaps 3,000 times as potent as mescaline (O'Brien, 2011), but weaker than the synthetic hallucinogen DOM/STP (Schuckit, 2006a). The LSD molecule is

¹¹To avoid confusion, these compounds will continue to be referred to as hallucinogens.

¹²See Appendix 4.

water-soluble, making it possible for it to be both rapidly and completely absorbed from the gastrointestinal tract when it is ingested (Tacke & Ebert, 2005). Once in the circulation, LSD is distributed to all blood-rich organs in the body, and only a small percentage of the original dose is thought to reach the brain (Tacke & Ebert, 2005). In the brain, LSD appears to function as a serotonin agonist (Jenkins, 2007; Klein & Kramer, 2004), especially at the 5-HT_{2a} receptor site, although it also seems to have action at dopamine and adrenalin receptor sites (Garcia-Romeu et al., 2016; Glennon, 2004; Halberstadt, 2017).

The highest brain LSD concentrations are found in the regions associated with vision, the limbic system, and the **reticular activating system (RAS)**.¹³ In retrospect, this should not be surprising, since these regions of the brain are involved in the process of interpreting and the emotional response to perceptions of reality. LSD appears to alter the normal function of serotonin in the dorsal midbrain raphe region of the brain (Hobson, 2001; Jenkins, 2007). By binding at the 5-HT_{2a} receptor sites in this region, LSD is able to indirectly activate **acetylcholine**¹⁴-based neurons that suppress rapid eye movement (REM) sleep during the waking state. This allows those neurons to then become active, allowing perceptual and emotionally charged images normally seen only during sleep to slip over into the waking state as well as inducing the perceptual distortions and emotions characteristic of the LSD experience (Hobson, 2001; Jenkins, 2007). Tolerance to LSD's effects develops rapidly, often after just 2–4 days of continuous use (Evans et al., 2005; Jones, 2005). After tolerance develops, the individual must abstain from additional hallucinogen use for 2–4 days to allow the tolerance to abate before restarting using LSD (Jones, 2005). Cross-tolerance between hallucinogens is common, so the individual must abstain from all hallucinogen use during this time. There is no known withdrawal syndrome from LSD (Fadem, 2009). Scientists have yet to determine the lethal dose of LSD, making it perhaps the safest compound known to modern medicine (Erickson, 2007; Pechnick & Ungerleider, 2004; Ross, 2012).¹⁵ Death in LSD abusers is rare and usually is the result of the perceptual distortions induced by LSD (Drummer & Odell, 2001; Pechnick & Ungerleider, 2004). This is not to imply that LSD is entirely safe. There

are reports suggesting that LSD-induced seizures might occur up to 60 days after the individual's last use of this compound, although the causal mechanism for such seizures remains unknown (Klein & Kramer, 2004).

The biological half-life of LSD is estimated to be approximately 2.5 to 3 hours (Jenkins, 2007; Oehmichen, Auer, & Konig, 2005). It is rapidly biotransformed in the liver, with only 1–3% of a single dose of LSD excreted from the body unchanged. The rest is eliminated in the bile (Drummer & Odell, 2001; Tacke & Ebert, 2005). The biotransformation/elimination process is so rapid that the major metabolite of LSD, 2-oxy-LSD, remains in the individual's urine for only 12–36 hours after it is ingested. While individuals who use illicit drugs often claim that the LSD detected in their urine was a result of passive absorption through the skin, there is little evidence that this is possible. The subjective effects of LSD last far longer than its biological half-life, and for the typical individual, the perceptual distortions usually last for 12–18 hours after the drug is first ingested (Drummer & Odell, 2001; Garcia-Romeu et al., 2016; Weiss, 2007). The discrepancy between the drug's duration of effects and its elimination half-life might reflect the fact that some individuals ingest large doses, thus allowing residual LSD to remain in their bodies, or that the substance-induced equilibrium in the balance of neurotransmitters requires several days to be reestablished.

The Subjective Effects of LSD

The subjective effects of LSD begin about 5–10 minutes after the dose is ingested. The negative effects include such symptoms as anxiety, gastric distress, increased blood pressure, tachycardia, increased body temperature, dilation of the pupils, nausea, muscle weakness, exaggerated muscle reflexes,¹⁶ dizziness, and possible muscle tremor (Tacke & Ebert, 2005). These effects are usually easily tolerated by the individual with LSD use experience. LSD-induced hallucinations or perceptual distortions begin 30–60 minutes after the drug is ingested, last at full intensity for 2–4 hours, and gradually wane over the next 8–12 hours (O'Brien, 2006; Pechnick & Ungerleider, 2004).¹⁷ The individual's subjective interpretations of LSD's effects are thought to reflect his/her (a) personality,¹⁸ (b) expectations, (c) the environment in

¹³See Glossary.

¹⁴See Glossary.

¹⁵Obese (2007) discussed an incident from the year 1962 in which a trio of scientists injected an elephant at the Denver zoo with a dose of LSD estimated to be 3,000 times the typical dose used by a human. For unknown reasons, the elephant died within one hour. The results of this study do suggest that it is possible to die from an LSD overdose. Why the scientists decided to inject the elephant with LSD has never been revealed.

¹⁶Known as *hyperreflexia*.

¹⁷Weiss (2007) suggested that some individuals might simultaneously use cocaine or an amphetamine compound to prolong the effects of LSD.

¹⁸In this context, there is some evidence suggesting that LSD reinforces preexisting mood states, which are a reflection of the person's core personality.

which the drug was used, and (d) the dose ingested (Tacke & Ebert, 2005; Weaver & Schnoll, 2008).

Individuals who use this substance often refer to the LSD experience as a “trip,” during which they might experience a sensation of having no psychological boundaries, enhanced insight, a heightened awareness of sensory perceptions, enhanced memory recall, a feeling of contentment, and a sense of being “at one” with the universe (Callaway & McKenna, 1998). The trip is made up of several distinct phases: The first phase, which begins within a few minutes, is experienced as a release of inner tension. During this phase, the individual using LSD might feel the need to laugh or cry, and may experience a sense of euphoria (Tacke & Ebert, 2005). Stage two begins between 30 and 90 minutes after the drug is ingested, and will involve sensations such as perceptual distortions, **synesthesia**,¹⁹ and visual illusions (Pechnick & Ungerleider, 2004; Sacks, 2008; Tacke & Ebert, 2005; Traub, 2009). The third phase of the LSD experience begins 3–4 hours after the drug is ingested, and during this phase the individual experiences a distortion of the sense of time. Some individuals report a sense of ego disintegration and anxiety/panic reactions, which could trigger a “bad trip” experience from LSD and contribute to even more anxiety on the part of the user. During this phase, the individual might express a belief that s/he has quasi-magical powers, or that they are somehow in control of events around them (Tacke & Ebert, 2005). Such beliefs are potentially fatal, as those who use LSD have been known to jump from windows or operate motor vehicles during this phase. The possibility that someone using LSD might experience suicidal thoughts or even attempt suicide is controversial, but Krebs and Johansen (2015) reported that after examining the records of 130,000 U.S. adults, including 19,299 who acknowledged hallucinogen use, they failed to find that those who used psychedelic substances were more likely to experience current mental health problems, although there was a tendency for those who have used a psychedelic to report a depressive episode before the age of 18.

The effects of LSD normally start to wane 4–12 hours after ingestion (Garcia-Romeu et al., 2016; Pechnick & Ungerleider, 2004). As the individual begins to recover, s/he will experience periods of normal perception, interspaced with periods in which the individual continues to experience residual effects of LSD, until eventually s/he is again fully in touch with reality. Following the last phase of the LSD trip, the individual might experience a residual sense of emotional numbness that might last for hours to days.

The “Bad Trip”

Those who use LSD often experience anxiety or outright panic reactions, which is often referred to as a “bad trip.” Although it was once thought that only those inexperienced at using LSD were prone to such reactions, it is now known that even those with experience with LSD are vulnerable to a bad trip. Several factors that seem to influence the probability and course of a bad trip: (a) the individual’s expectations for LSD, (b) the setting in which LSD is used, and (c) the psychological health of the user (Strassman, 2005). Feedback from others also influences how the individual interprets the drug’s effects.²⁰ If the individual does develop an LSD-related panic reaction, s/he will usually respond to calm, gentle reminders from others that the feelings are a reaction to the drug, and that they will pass. This is known as “talking down” the individual using LSD.

Pharmacological intervention is necessary only in the most extreme cases,²¹ and there is evidence that the “atypical” antipsychotic medications clozapine and risperidone bind to the same receptor sites utilized by LSD, aborting the drug trip within 30 minutes of the time that either compound is administered (Walton, 2002). Although some physicians advocate the use of diazepam as an anxiolytic for such reactions, diazepam might further distort the individual’s perception of reality, contributing to even more anxiety for the individual. Normally, benzodiazepine-induced sensory distortion is so slight as to be unnoticed by the typical patient, but, when combined with the effects of LSD, might become quite substantial and contribute to the problem being treated.

Even without treatment, the LSD-related bad trip will last only 6–12 hours at most, and will resolve as the drug’s effects wear off (Garcia-Romeu et al., 2016; Jones, 2005). On rare occasions, however, LSD seems to “activate” a latent psychosis within the individual, compounding the problem of treatment for that person (Erickson, 2007; Garcia-Romeu et al., 2016; Tacke & Ebert, 2005). However, it is unclear whether this activation hypothesis is accurate, since the “LSD experience is so exceptional that there is a tendency for abusers to attribute *any* later psychiatric illness to the use of LSD”

²⁰The individual who provides such feedback is often called “ground control,” and is usually not abusing LSD at the time that he or she functions in this role.

²¹On occasion, physicians will encounter a patient who took LSD mixed with belladonna or another anticholinergic compound. If the physician were to attempt to treat the patient’s anxiety and agitation with a phenothiazine (an older class of antipsychotic medications), the combination of these compounds might induce a coma, or even death from cardiorespiratory failure. This is one reason the attending physician should be alerted about what compound(s) have possibly been ingested by the patient, and if possible provided with a sample of the drug(s) ingested, so that he or she might avoid potentially dangerous chemical interactions.

¹⁹See Glossary.

(Henderson, 1994, p. 65, *italics added*). As the author points out, psychiatric disorders that manifest weeks, months, or even years after the individual's last use of LSD are often attributed to hallucinogen use, even if this took place months prior to the first expression of a psychiatric disorder.

It has been suggested that LSD functions as a selective neurotoxin, destroying the neurons that inhibit excessive stimulation of the visual cortex (Gitlow, 2007). There is a need for further research into this possibility. In spite of the claims of some drug dealers, it is possible to overdose on LSD, although this is quite rare. Symptoms seen in an LSD overdose include convulsions and **hyperthermia**,²² as well as an exaggeration of the normal effects of LSD. As is true for *any* suspected drug overdose, immediate medical care is imperative.

The LSD “Flashback”

A “flashback” is period of perceptual distortion similar to those experienced during LSD use, but during a period when the individual has not used a hallucinogen. The first clinical reports of hallucinogenic-related “flashbacks” are more than 100 years old (Jones, 2005). These cases involved persons who had used mescaline, and who continued to experience sensitivity to light, shade, or sounds for extended periods after their last use of the compound. The symptoms of the LSD-related flashback²³ fall into one of three categories: (a) perceptual, (b) somatic, or (c) emotional issues, as well as feelings of depersonalization. Depersonalization flashbacks may involve the individual reexperiencing distressing emotions first experienced when the individual used LSD (Weiss & Millman, 1998). Reported symptoms include visual field distortions, hallucinations, “flashes” of light or color, halos surrounding objects in the visual field, and the perception that things are growing larger or smaller (Pechnick & Ungerleider, 2004). Between 5 and 77% of individuals who use LSD will experience at least one flashback (Garcia-Romeu et al., 2016), which can be a source of anxiety for the individual inexperienced in using LSD and who is unprepared for this phenomenon. Those experienced in the use of LSD might not report flashbacks unless specifically questioned about these experiences, accepting them as a normal consequence of their LSD use (Batzner, Ditzer, & Brown, 1999).

²²See Glossary.

²³Although a common consequence of LSD use, similar experiences might occur in patients with cerebral lesions, infections, a form of epilepsy that causes visual field disturbances, or delirium. Thus, a physician should be consulted in cases of suspected LSD flashbacks to determine whether the patient might have another cause of what appears to be a LSD-related “flashback.”

The exact mechanism behind the LSD flashback experience remains unclear at this time, but it is recognized by the American Psychiatric Association (2013) as a real phenomenon, called hallucinogen persisting perceptual disorder (HPPD), in cases where the flashbacks continue to occur over extended periods of time (Drummer & Odell, 2001; Garcia-Romeu et al., 2016; Pechnick & Ungerleider, 2004). Clinical evidence suggests that the LSD-related flashback experiences most commonly occur in the first 6 months following the individual's last use of LSD, although they have been reported to occur up to 5 years after the individual's last episode of use (Jones, 2005). In rare cases, it remains a permanent aftereffect of the individual's LSD use (Gitlow, 2007). It was once thought that the flashback required repeated episodes of LSD use, but clinical experience has revealed that even those using LSD only one time have had flashback experiences (Evans et al., 2005; Pechnick & Ungerleider, 2004). Flashbacks might be triggered by such things as stress, fatigue, marijuana use, emerging from a dark room into the light, infections, and the use of CNS stimulants (Jones, 2005; Weaver & Schnoll, 2008). Armed with this knowledge, some persons will intentionally try to experience a flashback to experience and enjoy the effects of the phenomenon. The use of sedating agents like alcohol can also trigger flashbacks for unknown reasons (Batzner et al., 1999).

Treatment for the LSD-related flashback is usually limited to simple reassurance that the experience will last for a short time (usually hours, but sometimes longer), and that it is a normal consequence of LSD use (Sadock et al., 2015). If reassurance is not sufficient in some cases, the use of **anxiolytic**²⁴ medications is useful for acute flashback-related anxiety.

Drug Interactions Involving LSD

Unfortunately, there has been little clinical research into the possible drug interactions between LSD and other compounds. There are case reports suggesting that the selective serotonin reuptake inhibitor (SSRI) antidepressants might trigger or exacerbate LSD-related flashbacks (Ciraulo, Shader, Greenblatt, & Creelman, 2006). There are reports of LSD/SSRI-induced grand mal seizures, although it was not known whether this was a drug-induced seizure or a seizure caused by another factor. LSD can interact with the antiviral agent ritonavir, used in the treatment of HIV infection,²⁵ resulting in higher blood concentrations of LSD, with unknown consequences (Weiss, 2007). There are other potential interactions between LSD and other compounds, but there has been little research into this area.

²⁴See Glossary.

²⁵Discussed in Chapter 34.

Section Summary

LSD has long been viewed as the prototypical hallucinogen. It is a very potent compound that affects multiple neurotransmitter systems in the brain, although its primary effects are thought to be caused by its ability to influence the serotonin neurotransmitter system. Originally discovered by accident, it was briefly investigated by various governmental agencies as a possible chemical warfare agent. Its use became popular in the 1960s, and its popularity has waxed and waned since then. In spite of many years of research into this compound, there is still a great deal to be discovered about LSD.

Phencyclidine (PCP)

Phencyclidine (PCP) was first introduced in 1957 as an experimental surgical anesthetic designed for intravenous administration (Tacke & Ebert, 2005), and the first reports of PCP misuse began to appear in the clinical literature around 1965 (Javitt & Zukin, 2005). As a surgical anesthetic, PCP was found to induce problems such as agitation, a drug-induced delirium, and/or a psychotic reaction that lasted up to 10 days. These reactions made recovery from surgery difficult, and its use in humans was quickly discontinued (Javitt & Zukin, 2005; Jenkins, 2007; McDowell, 2004). It still was used as a veterinary anesthetic agent in the United States until 1978, when all legal production of phencyclidine in the United States was discontinued. It has since been classified as a Schedule II compound.²⁶ It is still legally manufactured by pharmaceutical companies in other countries, as it is used as a veterinary anesthetic in other parts of the world.

By the time its use as a surgical anesthetic in the United States had been discontinued, those who use illicit drugs had discovered PCP. It has never been a popular drug of misuse in this country, and the level of its use has waxed and waned over the years (Javitt & Zukin, 2005). However, it is still occasionally misused by some persons, and it is a common adulterant added to other drugs. For these reasons, we will review the effects of phencyclidine.

Scope of Phencyclidine Abuse

Currently, phencyclidine is not a popular drug to misuse, and its use outside of this country is rare (Mozayani, 2009). However, there has been an increase in recent years, despite decline in use in the 1980s and 1990s (DEA, 2013). Even in the United States, *intentional* PCP use is uncommon (Zukin, Sloboda, & Javitt, 2005). However, it is often found as an adulterant in other compounds or is sold as other

drugs, resulting in unintentional PCP exposure that might cause significant anxiety for the unsuspecting individual using drugs. In addition to these side effects is possible drug-induced anxiety that intensifies the individual's distress and that compounds the side effects noted below (Zukin et al., 2005). It is thought that less than 2.4% of those 12 and over in the United States has ever used PCP (SAMHSA, 2016).

Methods of PCP Administration

PCP might be used intranasally, ingested orally, injected into either muscle tissue or intravenously, and when mixed with other substances it might be smoked (Karch, 2009). Smoking is the most popular method of PCP use, as it allows the individual to titrate their total PCP intake to a suitable level, after which time they can just discontinue further PCP smoking for a few minutes, hours, or days.

Subjective Experience of PCP

When used, PCP's effects have been found to last for several days. During this time, the individual will experience rapid fluctuations in his/her level of consciousness, a sense of dissociation in which reality appears to be distorted or distant, euphoria, decreased inhibitions, a feeling of immense power, analgesia, an altered sense of time, and a loss of sensation in or the feeling that body parts are no longer attached to the abuser's body (Brust, 2004; Weaver, Jarvis, & Schnoll, 1999). Some of these experiences can be rather frightening to the individual not experienced in PCP use, inducing a panic reaction. Other reported symptoms include disorientation, confusion, assaultiveness, irritability, depression (which might reach the level of suicidal thinking or acts), and paranoia. As the list of PCP-induced effects would suggest, many of these effects are not desired by the abuser, and many abusers attempt to control them through simultaneous use of other compounds. Unfortunately (from the perspective of the individual using PCP), tolerance to PCP's euphoric effects develops rapidly (Javitt & Zukin, 2005). To overcome this tolerance, some individuals will go on PCP-free "holidays" (avoiding the use of PCP for days or weeks), while others will increase their dose to possibly dangerous levels.

The Pharmacology of PCP

Since it is an illicit compound in this country, the phenomenon of PCP use or dependence have not been studied in detail (Zukin et al., 2005). Much of what is "known" about PCP and its effects is based on anecdotal case reports involving PCP use, or on the limited experience with phencyclidine as an experimental anesthetic agent. Virtually nothing is known about PCP dependence or whether there is a withdrawal syndrome for this compound.

²⁶See Appendix 3.

Chemically, PCP is a weak base, soluble in both water and blood lipids. Because it is a weak base, it will be absorbed through the small intestine when ingested, resulting in a slower onset of the drug's effects than when it is smoked (Zukin et al., 2005). Orally administered doses of PCP begin to manifest in 20–30 minutes after the drug is ingested, but there is a great deal of intraindividual variability in both the onset of the drug's effects in the oral abuser and the duration of its effects after ingestion. When smoked, the effects begin to manifest in 2–3 minutes (Schnoll & Weaver, 2004). The effects of a small dose of orally administered PCP usually last 3–4 hours, while the peak effects of smoked PCP are achieved in 15–30 minutes, and last for 4–6 hours after a single dose (Jenkins, 2007). Much of the PCP that is smoked is destroyed in the smoking process, the result being that only 30–50% of the available PCP smoked actually reaches the circulation.

Because of its lipid solubility, PCP tends to accumulate in body tissues with a high concentration of lipids, such as the brain (Scholl & Weaver, 2004). Measured levels of PCP in the brain might be 10–113 times as high as the blood plasma levels (Zukin et al., 2005). Once in the blood, PCP interacts with a number of different neurotransmitter receptor sites, acting as an antagonist for N-methyl-D-aspartic acid (NMDA) (Jenkins, 2007; Zukin et al., 2005). PCP also functions as a sigma opioid receptor agonist, and since activation of this receptor site causes dysphoric effects, this seems to be the mechanism through which PCP causes such unpleasant effects (Brust, 2004; Drummer & Odell, 2001). It also binds at some of the endogenous cannabinoid receptor sites, and this is assumed to be the mechanism by which it can cause hallucinations (Glennon, 2004).

The effects of PCP on the individual's brain vary, depending on such factors as experience with the drug, expectations, and the drug concentration in the brain. Depending on the concentration of PCP in the brain, it might function as an anesthetic, stimulant, depressant, or hallucinogenic compound. At about 10 times the minimal effective dose, PCP begins to function as a monoamine reuptake blocker, blocking the action of neurotransmitters such as dopamine and norepinephrine, and inducing euphoria for the user. Depending on the concentration of PCP in the brain, it also may alter the normal function of the **NMDA/glutamate** receptor²⁷ in the brain, which might account for the excitement and agitation seen in some individuals who use PCP (Traub, 2009).

The typical illicit drug dose is approximately 5 mg. However, product potency in illicit drugs is always a problem, and so it is impossible to predict in advance how much PCP is in a designated tablet without special testing. Most of a single

dose of PCP is biotransformed by the liver into a number of inactive metabolites, which are then excreted by the kidneys, and only about 10% of a single dose is excreted unchanged (Karch, 2009). The PCP half-life is about 20 hours, although there is a great deal of intraindividual variability in this figure (Jones, 2005). This estimate is based on the assumption that the individual ingested just one 5-mg dose of PCP; if the individual has used an exceptionally large dose of PCP, the half-life might be extended to as long as 72 hours. Following a PCP overdose, the half-life might be as long as several weeks. One reason for this is the affinity of the PCP molecule for lipid molecules, which allows for significant stores of PCP to accumulate in the body's fat tissues, which slowly "leak" back into the general circulation over time.

Physicians once believed that it was possible to reduce the half-life of PCP by making the urine very acidic. This was accomplished by having the patient ingest large amounts of ascorbic acid or cranberry juice. However, it has since been discovered that this practice may cause myoglobinuria and possible kidney failure, and it is no longer recommended as a treatment for PCP overdoses (Brust, 2004). Although PCP is biotransformed at a relatively steady pace, heavy exercise, diet, or major injury might cause significant amounts of PCP to be released back into the circulation of the individual who has heavily used the drug, possibly inducing a PCP flashback experience (Schuckit, 2006a). In the next section, we will look at some of the known complications of PCP use.

Complications of PCP Use

Phencyclidine is a dangerous compound with a narrow therapeutic window. Some of the complications of PCP use are reviewed in Table 12-1.

PCP-related death might be either a direct or indirect outcome of the drug's use. Following even mild levels of PCP intoxication is a period of adjustment that may last 24–48 hours, which may be prolonged in cases where the person ingested an exceptionally large dose. During this adjustment period, the individual will gradually "come down," or return to a normal level of function. Those who acknowledge chronic PCP use report social withdrawal and feelings of depression following their last episode of phencyclidine use. A mild withdrawal syndrome following periods of prolonged PCP use has been reported by some individuals. Many individuals report having memory problems, which seem to resolve after they stop abusing this compound. This is consistent with evidence that PCP can cause neural **necrosis**²⁸ in the hippocampus (Javitt & Zukin, 2005). It is not known at this time

²⁷See Glossary.

²⁸See Glossary.

TABLE 12-1 Known Complications of PCP Abuse

Dose of: 1–5 mg	5–10 mg	10–25 mg or higher
Aggression	Analgesia	Arrhythmias (possibly fatal)
Alcohol-like intoxication	Aggression	Analgesia/anesthesia
Anxiety	Anxiety (may be severe)	Coma (possibly with the eyes open)
Ataxia	Depersonalization	Death
Body image distortion	Euphoria	Encopresis
Confusion	Hypersalivation	Hallucinations (both visual and tactile hallucinations reported)
Distorted sense of time	Increased muscle strength	
Euphoria	Lethargy	Hypertension (possibly causing strokes or other damage to user's body)
Hallucinations (usually visual, but other forms of hallucinations also reported)	Memory impairment	Paranoia
	Nystagmus	Reduced reaction time
Nystagmus	Paranoia	Respiratory depression/arrest
Periods of rage	Psychosis (drug induced)	Rhabdomyolysis
	Sweating	Seizures

SOURCES: Based on information in Javitt and Zukin (2005); Mozayani (2009); Wilson, Shannon, and Shields (2017), Sadock et al. (2015); Tomb (2008).

what degree of recovery, if any, is possible from PCP-related brain damage.

Another possible complication of PCP use is a drug-induced psychosis. In the case of PCP, this psychosis appears to progress through three different stages. The first stage of PCP-induced psychosis is the most severe, and includes symptoms such as paranoid delusions, anorexia, insomnia, and unpredictable assaultiveness. During this phase, the individual is exceptionally sensitive to external stimuli such as bright lights or loud sounds, and the “talking down” techniques so effective with LSD bad trips will not work with patients in a PCP-induced psychosis. Restraints are occasionally necessary to prevent the patient from harming him/herself or others during this phase.

The second stage of PCP psychosis is marked by continued paranoia and restlessness, but the individual is usually calmer and in intermittent control of his/her behavior. This phase usually lasts around 5 days, and gradually blends into the final phase of PCP psychosis. While the PCP psychosis is usually time-limited, in some cases recovery might take months, or even years. The final phase usually lasts 7–14 days, during which time the individual gradually returns to a normal state of mind. In many cases, individuals then experience an episode of depression.

PCP Use as an Indirect Cause of Death

PCP-induced hypertensive episodes might last for as long as 3 days after the individual’s last use of PCP, placing stress

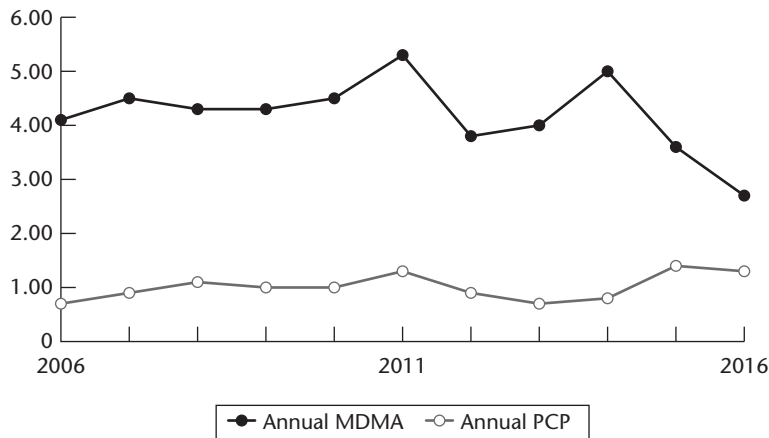
on the cardiovascular system during that time (Brust, 2004). Also, PCP-related periods of aggression have been identified as a factor in drug-related homicides with either the perpetrator or the victim being under the influence of PCP when the homicide was committed. PCP can induce seizures, exposing the individual to the same potential for death as found in typical seizures, and indirectly causing the user’s death through this process. Finally, the dissociative and anesthetic properties of PCP can cause or exacerbate traumatic injuries, possibly contributing to the individual’s death. Given this litany of undesirable effects, it is a mystery why people might choose to use this compound. However, as noted earlier in this chapter, phencyclidine continues to lurk in the shadows, and has seen a recent slight upswing in use.

Ecstasy (MDMA)

Prevalence of PCP Use Compared to MDMA

The compound N-alpha-dimethyl-1,3-benzo-dioxole-t-ethanamine²⁹ (MDMA) is a much more popular hallucinogen than PCP among high school students, as evidenced by the data summarized in Figure 12-1.

²⁹Like many chemical compounds, there are multiple ways to represent the chemical structure of the same chemical. An alternative way to describe MDMA is 3,4-methylenedioxy-methamphetamine (Simek, 2015).



Note: Survey wording changed in 2014 to include “Molly”, a commonly used street name for MDMA.

FIGURE 12-1 Percentage of High School Seniors Using PCP or MDMA

SOURCE: Johnston, O'Malley, Miech, Bachman, and Schulenberg (2017).

A Short History of Ecstasy (MDMA)

MDMA was first isolated in 1912, with a patent on the compound being issued in 1914 (Schuckit, 2006a). Chemists had hoped that the compound would function as an appetite suppressant; however, subsequent research failed to support this theory and researchers quickly lost interest in MDMA. It remained only a laboratory curiosity until the early 1950s, when the U.S. Army asked the University of Michigan to determine its toxicity as part of a preliminary assessment as a possible chemical warfare agent (Karch, 2009). However, the decision was made not to pursue further research into this compound by the army, and it returned to chemical obscurity.³⁰

In the mid-1960s, a small number of psychotherapists suggested that MDMA might be useful as an adjunct to psychotherapy. Research into this application of MDMA ended in 1985 when, in spite of testimony by physicians and the recommendation of an administration law judge, the Drug Enforcement Administration (DEA) classified MDMA as a Schedule I³¹ rather than a Schedule III compound (Gahlinger, 2004; Mithoefer, 2011; Shulgin & Shulgin, 2007). Only a quarter of a century later, limited research into the possible application of MDMA as an adjunct to psychotherapy again was being conducted in both the United States and Europe (Mithoefer, 2011).

³⁰It has emerged, however, as a possible adjunct to the treatment of at least some forms of posttraumatic stress disorder (PTSD) (Mithoefer et al., 2013; Mithoefer, Mithoefer, & Wagner, 2008). Further research into possible medical applications of MDMA is under way at this time.

³¹See Appendix 3.

Unfortunately, in a pattern that is eerily similar that seen with LSD a decade earlier, the 1960s MDMA escaped from the laboratory to become a drug of misuse. However, it was quickly overshadowed by LSD, which was both more potent and did not induce the nausea or vomiting experienced by many who used MDMA. Those who used illicit drugs began to become interested in MDMA in the mid-1970s, in part because it was not then classified as an illegal substance. Drug suppliers began to market it as a commercial venture, engaging in premarketing discussions about possible product names, much as an automotive company would for a new vehicle. The name “ecstasy” was eventually selected for this compound, a demand for the product was generated, and a supply/distribution network set up to meet the demand (Karch, 2009; McDowell, 2004). The original samples of MDMA even contained a “package insert” (Karch, 2009) that was filled with psychobabble, and that gave suggestions about the best ways to use MDMA. Within the span of a few years, MDMA became a popular drug to misuse in both Europe and the United States, and, as noted above, was eventually classified as a Class I drug. The DEA has approved research in certain situations, including the use of MDMA for PTSD, as well as more recently in patients with life-threatening diseases for related anxiety. There is the potential that in coming years, MDMA may be legally prescribed for certain conditions. MDMA has remained a popular drug to misuse, as evidenced by the fact that there are more than 150 known street names for this compound (Kilmer, Palmer, & Cronce, 2005). In recent years, the name “Molly” has gained popularity.

Scope of MDMA Misuse

Worldwide production of MDMA is on the rise, and exceeds the amount seized globally each year (9 metric tons per year seized); globally, 19.4 million persons between the ages of 15 and 64 years are thought to have used MDMA at least once in the preceding 12 months (U.N. Office on Drugs and Crime, 2017). In the United States, 6.8% of those 12 and older are thought to have used MDMA at least once, and 1% are thought to have done so in the past 12 months (SAMHSA, 2016). MDMA is a popular illicit drug with young people, with 4.9% of high school seniors in the United States reporting having used this compound at least once, with 2.7% indicating use in the past year (Johnston, O'Malley, Miech, Bachman, & Shulenberg, 2017).

It was originally thought that MDMA was harmless, a myth that helped it to find widespread acceptance by a subculture devoted to loud music and parties devoted to the use of MDMA, similar to LSD parties of the 1960s (Ramcharan et al., 1998). Such parties, called “raves” at the time,³² first began in Spain, spread to England and across Europe, and then to the United States (McDowell, 2004; Rochester & Kirchner, 1999). While these parties have become less common, MDMA has moved into mainstream nightclubs, especially those popular with older adolescents and young adults (Morton, 2005).

Patterns of MDMA Misuse

There is a great deal of interindividual variability in dosing levels because of (a) the unknown potency of the tablet/powder being used, and (b) the individual's tolerance to MDMA, with greater adverse effects occurring in females (Vizeli & Liechti, 2017). Some tablets purporting to be MDMA have been found to contain no MDMA at all, while others might contain 100 mg (Virani, Bezchlibnyk-Butler, & Jeffries, 2009). This variability between tablets makes it very easy for the individual to overdose, which will be discussed later in this section. The typical user of MDMA attempts to ingest 60–120 mg³³ at a time (Outsley, 2006). Those who use this substance usually engage in episodic MDMA use to allow themselves to recover from the drug's effects³⁴ (Evans et al., 2005; Gouzoulis-Mayfrank et al., 2000). Ecstasy does appear to have a “ceiling effect,” beyond which the individual will not achieve more euphoria but will be vulnerable to the negative effects of the compound (Bravo, 2001). Although episodic use is the norm

for MDMA, those who binge with MDMA have been known to take as many as 5–25 tablets³⁵ in a short period of time, and some users of MDMA report a total lifetime consumption of up to 40,000 tablets (Lawton, 2009). These facts demonstrate how desirable its effects are for some persons.

Pharmacology of MDMA³⁶

Technically, MDMA is classified as a member of the *phenethylamine* family of compounds, but its chemical structure is also very similar to that of the amphetamines, and some neuropharmacologists classify it as a hallucinogenic amphetamine. For the sake of this chapter, it will be classified as a hallucinogenic compound, since this is the context in which it is most commonly used. It is usually used in tablet form, although there is a growing tendency for MDMA powder to be sold, since it is easier to produce the powder than to form it into a tablet (Boyer, 2005). The use of such powder raises the potential for a lethal overdose, however, since it is difficult to judge the total dose being used by the individual (Lawton, 2009). There are also reports of intravenous usage (Garcia-Romeu et al., 2016).

The pharmacokinetics of MDMA are complicated by the fact that the way an individual's body metabolizes the substance based on genetics (Vizeli, Schmid, Prestin, Meyer Zu Schwabedissen, & Liechti, 2017). There has been little research into the effects of traditional MDMA on the human brain (Lawton, 2012a, 2012b), and only limited research into how the body responds to the compound. So the information that follows is tentative, and may be revised as scientists discover more about the pharmacokinetics of each form of the MDMA molecule.

One of the few studies exploring the effect of MDMA on the human brain was carried out by Wardle, Kirkpatrick, and de Wit (2014). The authors of this study administered standard doses of MDMA to volunteers and then exposed them to a series of photographs judged to be emotionally positive, neutral, and negative. The authors found that, as expected, the positive pictures elicited a positive emotional response, but unexpectedly that their emotional response to the negative photos was more blunted and less negative, suggesting that this is the mechanism through which MDMA might facilitate interpersonal psychotherapy by negating some of the more traumatic memories from the individual's past.

³²Welch (2013) suggested that this term has been replaced by the phrase “dance-music festival.”

³³Although this is based on the theory that the MDMA ingested is pure and not adulterated.

³⁴Although those who use multiple substances might continue to misuse other compounds during these periods of abstinence.

³⁵The potency of illicit MDMA tablets varies from one batch to the next, and so the actual dose of MDMA being ingested by these individuals is not known.

³⁶This section is based on the assumption that the person ingested only one (1) dose of MDMA. Many individuals consume multiple doses over extended periods (8 to 12 hours), altering the pharmacokinetics of this compound. Higher doses result in higher plasma levels of MDMA, for example, producing both stronger effects and greater exposure to contaminants in the compound ingested (Ricaurte, Langston, & McCann, 2008).

Ecstasy is well absorbed from the gastrointestinal tract, and thus the most common method of use is through oral administration. The effects of an oral dose begin within 20–60 minutes of ingestion, and peak about 1–4 hours later (de la Torre et al., 2004; Garcia-Romeu et al., 2016; Gonzalez, Vassileva, & Scott, 2009; Karch 2009; MacLean et al., 2015; McDowell, 2004, 2005; Virani et al., 2009). MDMA is extensively biotransformed in the liver, and the elimination half-life has been estimated to be about 8 hours for the normal person (Karch, 2009; Tacke & Ebert, 2005; Virani et al., 2009). It is important to keep in mind that some persons are slow metabolizers of MDMA and that the elimination half-life for MDMA might be longer, and the amount of MDMA necessary to induce toxicity in these persons is relatively low (Virani et al., 2009). There are two main metabolic pathways for MDMA, and during the process of biotransformation about 9% of a single dose of MDMA is biotransformed into the metabolite MDA, which is itself hallucinogenic (de la Torre et al., 2004). However, one study using a single human volunteer revealed that three-quarters of the MDMA ingested was excreted unchanged in the urine within 72 hours. This raises a question: Was this individual a slow metabolizer of MDMA, or is the belief that MDMA must be extensively metabolized³⁷ before excretion inaccurate? There is obviously a need for additional research into the pharmacokinetics of ecstasy to answer this question.

Because MDMA is highly lipid-soluble, it is able to easily cross the blood-brain barrier and enter the brain without significant delay. In the brain, MDMA functions as an indirect serotonin agonist, first forcing the release and then blocking the reuptake of serotonin, and to a lesser degree norepinephrine and dopamine (Gahlinger, 2004; McDowell, 2004, 2005; Mithoefer, 2011; Parrott, Morinan, Moss, & Scholey, 2004). MDMA use also triggers the release of neurohormones such as oxytocin, prolactin, and cortisol, all of which are involved in the process of pair bonding (MacLean et al., 2015; Mithoefer, 2011). Its effects are strongest in the limbic system of the brain (Erickson, 2007). In cases where the user of MDMA dies (which, as will be discussed later in this chapter, is a distinct possibility), the residual MDMA molecules are extensively redistributed around the body. Thus, postmortem blood levels of MDMA may not be the same as the blood levels of this compound at the time of the individual's death ("Pharmacokinetics of MDMA (ecstasy) studied," 2008). As the information in this section suggests, there is much that remains to be discovered about the effects of this compound on the healthy individual (Lawton, 2012a, 2012b).

³⁷Remember: The term *biotransformation* usually is limited to prescribed medications, and *metabolization* is used to discuss illicit drugs, although they are the same process.

Subjective and Objective Effects of MDMA Use

There are multiple methods for making MDMA. Specialized equipment and training in organic chemistry are both required to avoid the danger of contaminating the MDMA being manufactured by toxins. Beyond these requirements, MDMA is easily synthesized. Much of what was known about MDMA's effects were based on observations made by those misusing the substance, and now recent research studies involving volunteer participants receiving a measured dose of MDMA under controlled circumstances.

The subjective effects of MDMA can be divided into three phases: (1) acute, (2) subacute, and (c) chronic (Outslay, 2006). The subjective effects of MDMA during the acute phase are dependent on such factors as the setting in which the drug is used, the dose ingested, and the individual's expectations for ecstasy. At a dose of between 75 and 100 mg, individuals report experiencing a sense of euphoria, closeness to others, increased energy, mild perceptual disturbances such as enhanced color/sound perception, a sense of well-being, reduced defensiveness, and improved self-esteem (Bravo, 2001; de la Torre et al., 2004; Outslay, 2006). These effects begin to manifest about 30–60 minutes after MDMA is ingested, peak at about 75–120 minutes after it is first ingested, and last for 6–12 hours (Outslay, 2006). Some of the reported desirable effects of MDMA are identified in Table 12-2 (de la Torre et al., 2004; Kobeissey, et al., 2007; Outslay, 2006; Passie, Hartman, Schneider, Emrich, & Kruger, 2005; Virani et al., 2009).

However, these effects are achieved at a cost, for MDMA can also induce many undesirable effects, which are reviewed in Table 12-3 (Bravo, 2001; de la Torre et al., 2004;

TABLE 12-2 Perceived Benefits of MDMA Use

Euphoria
Increased empathy toward others
Emotional openness
Increased empathy toward others
Increased psychomotor energy
Increased self-confidence
Enhanced mood
Increased sex drive
Feelings of intimacy
Increased feeling of personal desirability as sexual partner
Belief that individual has improved self-awareness/insight
Intense feelings
Different state of mind/perceptions

TABLE 12-3 Possible Consequences of MDMA Abuse

Anxiety
Anorexia
Ataxia
Blurred vision
Bruxism (grinding of teeth)
Central venous sinus thrombosis
Confusion
Dissociation
Headaches
Heart palpitations
Hydration abnormalities (over- or under-hydrated)
Hypertension
Hyperthermia
Hypothermia
Loss of consciousness (various causes)
Motor tics
Muscle tension
Nausea/vomiting
Seizures, possibly leading to status epileptics (potentially fatal)
Subarachnoid hemorrhage
Sudden cardiac death
Urinary incontinence

Grob & Poland, 2005; Kobeissey et al., 2007; McDowell, 2005; Virani et al., 2009). The individual is more likely to experience one or more of these undesirable effects at higher dosage levels, although unpleasant effects are possible even at low doses (Grob & Poland, 2005). Individuals attempt to control the drug-induced bruxism by using a baby pacifier or candy to suck on after ingesting MDMA (Gahlinger, 2004; Klein & Kramer, 2004).

Surprisingly, although MDMA induces enhanced feelings of sexual arousal and attractiveness, habitual MDMA misuse has also been implicated as the cause of decreased sexual desire, and for men inhibition of the ejaculatory reflux, as well as erectile dysfunction (Finger, Lund, & Slagle, 1997; McDowell, 2004). Research has also found that individuals who misuse MDMA are more than *eight times* as likely to experience episodes of sleep apnea as are nonabusers (McCann, Sgambati, Schwartz, & Ricaurte, 2009). The authors suggested that this increased incidence of sleep apnea might be due to MDMA’s ability to function as a selective serotonin neurotoxin, since serotonin is implicated in the maintenance of normal respiration during sleep.

Following the period of acute MDMA misuse, there is an extended withdrawal period. The subacute phase begins 6–12 hours after the individual ingests MDMA, and in most cases lasts 1–7 days, although in extreme cases it can last for up to a full month (Outslay, 2006). This phase is also called *coming down* or the *hangover phase* (Outslay, 2006). Some of the symptoms experienced during this phase include fatigue, dry mouth, anorexia, insomnia, irritability, drowsiness, difficulty concentrating, and headache (de la Torre et al., 2004; McDowell, 2005; Morgan, 2006). It was once thought that the subacute phase of MDMA might also include feelings of depression, but Guillot and Greenway (2006) failed to find significant differences in the level of depression between a sample of MDMA abusers and MDMA-naïve subjects. This would cast doubt on the belief that the subacute stage of MDMA includes depression.

As the subacute phase tapers into the postwithdrawal phase, the individual will experience symptoms such as anxiety, depression, confusion, cognitive dysfunction, insomnia, irritability, low energy, and suspiciousness or outright paranoia (Outslay, 2006). These effects usually last for between 1 and 7 days, although in extreme cases they might continue for up to a month after the individual’s last MDMA misuse.

Complications of MDMA Misuse

MDMA has a reputation on the streets as a “safe” drug, an illusion supported by the lack of obvious consequences of abuse such as those observed in persons who have used methamphetamine, for example (Yudko & McPherson, 2009). The illusion of safety belies the fact that MDMA has an exceptionally small therapeutic window, with a significant overlap between the effective dose and the toxic dosage range (Karch, 2009; Outslay, 2006; Ropper & Brown, 2005). For example, animal research suggests that the lethal level of MDMA in humans is approximately 6,000 mg (Rosenthal & Solhkhah, 2005), a dosage level that, given the potency of some illicit MDMA samples, might be achieved after ingesting only 20–30 tablets (Lawton, 2009). However, fatal reactions to MDMA have been noted at doses far lower than this, and there is evidence that overdoses of MDMA are increasing in frequency and are under-reported by health care providers (Centers for Disease Control and Prevention, 2010a; Lawton, 2009).

In addition to the symptoms of MDMA toxicity reviewed in Table 12-3, individuals who have ingested toxic doses of ecstasy might possibly experience extreme (possibly fatal) elevations in body temperature, delirium, coma, hypotension, **rhabdomyolysis**,³⁸ and possible renal failure

³⁸See Glossary.

(de la Torre et al., 2004; Morton, 2005; Parrott et al., 2004; Rosenthal & Solhkhah, 2005; Zevin & Benowitz, 2007). As these symptoms clearly suggest, *any* real or suspected overdose of MDMA is a medical emergency requiring immediate medical intervention to avoid the danger of the patient's death. In the following section, we will examine some of the more specific dangers of MDMA abuse in detail.

MDMA-Related Cardiac Problems

It is now known that MDMA misuse can cause an increase in the heart rate, blood pressure, and the rate at which the heart muscle uses oxygen (Grob & Poland, 2005). MDMA misuse is a cause of cardiac arrhythmias such as potentially fatal ventricular tachycardia (Gahlinger, 2004; Grob & Poland, 2005; Karch, 2009; Klein & Kramer, 2004). One study of the hospital records of 48 patients who had been admitted to a hospital accident and trauma center following MDMA use found that two-thirds had heart rates above 100 beats per minute, or 38% higher than normal (Williams, Dratcu, Taylor, Roberts, & Oyefeso, 1998). It has been recommended that MDMA overdoses be treated with the same protocols used to treat amphetamine overdoses, with special emphasis placed on assessing and protecting cardiac function (Gahlinger, 2004; Rochester & Kirchner, 1999).

Animal research also suggests that MDMA functions as a cardiotoxin, causing inflammation of the heart muscle and damage to the left ventricle of the heart (Badon et al., 2002; Shenouda, Lord, McIlwain, Lucchesi, & Varner, 2008). In another study, the team of Patel and colleagues (2005) compared the heart muscle tissue samples of a group of deceased individuals who had used MDMA (as confirmed by toxicology tests) with those of deceased individuals who had not used MDMA of a similar age, and found that the hearts of the individuals who misused MDMA were on average 14% heavier than those who had not misused MDMA. This would appear to reflect the development of fibrous tissue within the cardiac muscle, which could interfere with the transmission of electrical signals in the heart necessary for maintenance of a normal cardiac rhythm. The development of fibrous tissue within the cardiac tissues would appear to reflect the cardiotoxic effects of MDMA (Klein & Kramer, 2004).

There is also evidence that chronic MDMA use can result in heart valve damage (Setola et al., 2003). The authors examined the impact of MDMA misuse on tissue samples in laboratories and found many of the same changes in heart valve tissue seen in the now-banned weight-loss medication fenfluramine.³⁹

³⁹After it was introduced, scientists discovered that this medication induced degeneration of heart valve tissue, prompting the manufacturer to withdraw it from the market.

Given the widespread use of MDMA, these research findings suggest the possibility of a future epidemic of MDMA-induced heart problems in those who are habitual users. Animal research does suggest that chronic MDMA misuse was associated with cardiac damage and potentially sudden cardiac death. The authors found that intracellular calcium levels were significantly higher in the hearts of MDMA-exposed rats than in MDMA-naïve rats. The concentration of calcium within the heart muscle cell helps to determine the rate and force at which it can contract. This appears to be the mechanism by which MDMA misuse can induce sudden cardiac death, or at least damage the heart muscle, according to the authors.

MDMA-Related Neurological Problems

The question of whether MDMA can cause or exacerbate neurological problems is rather controversial. Schilt and colleagues (2007) concluded that extended periods of MDMA misuse can result in cognitive decline. However, Krebs and Johansen (2008) challenged this conclusion on methodological grounds, pointing out that longitudinal research studies should answer this question more definitively than the retrospective studies, which are commonly used in research involving MDMA's effects on memory function.⁴⁰ Lawton (2009) observed that most individuals using MDMA also use other compounds, making the isolation of MDMA's effects rather difficult. To address this problem, Halpern and colleagues (2010) examined the performance on a neuropsychological test battery of 52 participants who acknowledged use of MDMA with minimal exposure to other drugs of misuse with that of 59 individuals who were not drug users. The authors found little evidence of neurocognitive deficits except in the area of impulse control, raising questions about whether the findings of earlier studies might have reflected the effects of other drugs being misused rather than MDMA itself. There are, however, case reports suggesting that some individuals using MDMA have suffered intracranial hemorrhage, while others have suffered occlusive strokes, both conditions that can also induce neurological damage.

A growing body of evidence suggests that MDMA use can cause a dose-dependent increase in cortical excitability (Bauernfeind et al., 2011). Cortical hyper-excitability was strongest in those persons with a greater lifetime level of MDMA, which might be one mechanism by which MDMA

⁴⁰Asking a person who has been misusing MDMA for 3 years, for example, to estimate how often they have used this compound might yield less accurate results than a longitudinal research study that examined how often the person misused MDMA on a week-by-week or month-by-month basis carried out over a 3-year period of time.

can induce seizures. The authors also found that chronic MDMA use can cause lifelong alterations in the physiology of the visual system in abusers, a finding that is of particular importance to those who have preexisting vision problems. This research is especially disturbing because the long-term implications of such cortical hyper-excitability and visual system changes are not known at this time. They might become permanent, or, following illicit drug use cessation, resolve to an unknown degree.

Further, there is a growing body of literature from both animal and human studies that suggests that MDMA can cause memory problems that may persist for weeks or even months after the individual's last use of ecstasy (McDowell, 2005; Morton, 2005; Yudko & McPherson, 2009). A rather frightening study conducted by Schilt and colleagues (2007) examined those who were new to MDMA misuse (<2 months), and found small but measurable cognitive deficits on the neuropsychological tests administered, and cognitive deficits are noted in patients who have ingested MDMA as infrequently as 20 times (Lawton, 2009). The cognitive deficits appear to be dose-related, with those who report higher levels of misuse being found to have higher levels of cognitive dysfunction in such areas as memory and verbal learning, as well as increased distractibility and a general loss of efficiency (Lawton, 2009; Lungvist, 2005; Quednow et al., 2006).

Those who misuse MDMA often report experiencing an insensitive to body temperature as they engage in heavy exercise, such as prolonged dancing. In extreme cases, this hyperthermia can cause the individual's death. Since hyperthermia is a symptom of the **serotonin syndrome**,⁴¹ this might be the mechanism by which MDMA is able to induce hyperthermia and dehydration in the abuser (Klein & Kramer, 2004). MDMA-related serotonin and dopamine release might also be a temperature-sensitive effect, with higher ambient temperatures being associated with higher levels of these neurotransmitters. Unfortunately, these neurotransmitters are involved in the euphoric sensations that many individuals who misuse MDMA seek, the result being that being in an area with a high ambient temperature might increase MDMA-induced pleasure, while simultaneously placing the individual's life at greater risk (O'Shea et al., 2005).

For reasons that are not well understood, MDMA appears to be able to lower the seizure threshold⁴² (Henry & Rella, 2001; Karch, 2009). This might reflect genetic vulnerability on the part of the patient experiencing an MDMA-related seizure, as there is evidence that patients who have

inherited two copies of what is known as the "short" serotonin transporter gene may be at greater risk for MDMA-related neurotoxicity (Roiser, Cook, Cooper, Rubinsztein, & Shakian, 2005). MDMA-related seizures also tend to be seen at higher dosage levels, although this is not a guarantee that lower doses will avoid the risk of seizures (Brust, 2004; Thompson, 2004).

As if all of this were not enough, there is strong evidence that MDMA functions as a selective neurotoxin that targets serotonergic neurons (Bauman & Rothman, 2007; Brust, 2004; McDowell, 2005). Animal research suggests that this effect can be seen at dosage levels used by human abusers (Ricaurte, Yuan, Hatzidimitriou, Branden, & McCann, 2002). While MDMA-related brain damage is more likely in persons who have ingested large doses of the compound, it is possible even on the occasion of the first dose (McDowell, 2005). The mechanism by which MDMA might function as a serotonin-specific neurotoxin is still not known, but preliminary evidence suggests that fluoxetine might protect the serotonin-based neurons from damage if ingested within 24 hours of the time that MDMA is ingested (Walton, 2002).

Although it was once thought that MDMA would place the individual at increased risk for Parkinson's disease later in life, this theory was later retracted (Brust, 2004; Yudko & McPherson, 2009). There is little evidence to support earlier beliefs that there was a relationship between MDMA abuse and subsequent development of Parkinson's disease (Morton, 2005; Yudko & McPherson, 2009). However, there is research data suggesting that MDMA might weaken the blood-brain barrier (BBB) for months, possibly years, after the last period of misuse (Vollmer, 2006). This would place the individual at increased vulnerability to various toxins and pathogenic organisms normally blocked by the BBB.

MDMA-Related Emotional Problems

There is evidence that those who misuse MDMA might experience flashback experiences similar to those seen after LSD abuse in the days following the MDMA use. Those who misuse MDMA are also sometimes forced to relive past experiences that they might not wish to face. This is the effect that made psychiatrists consider MDMA as a possible adjunct to psychotherapy in the 1960s. However, when an individual misusing MDMA is forced to reexperience these memories, there is usually no therapist to provide guidance and support, possibly adding an additional layer of trauma onto the original pain, which is potentially detrimental to the individual's mental health. MDMA misuse has also been linked with post-use anxiety attacks, persistent insomnia, irritability, rage reactions, and a drug-induced psychosis (Evans et al., 2005; Gahlinger, 2004; Karch, 2009; McDowell, 2005).

⁴¹See Glossary.

⁴²Seizures are potentially lethal through a variety of mechanisms, and thus MDMA-related seizures may indirectly add to the potential for the user's death.

MDMA-Related Gastrointestinal Problems

In Europe, where MDMA misuse was common in the 1990s, there were reports of MDMA-related liver toxicity and hepatitis. The exact relationship between MDMA misuse and the development of these liver problems is not known at this time. This might be the result of an idiosyncratic reaction on the part of a small number of persons, or a reaction to one or more contaminants mixed with the MDMA that was misused (Grob & Poland, 2002; Henry & Rolla, 2001).

Other MDMA-Related Problems

There are reports of MDMA-related rhabdomyolysis, possibly induced by heavy MDMA-induced exercise such as prolonged dancing (Gahlinger, 2004; Grob & Poland, 2005; Karch 2009; Klein & Kramer, 2004). While MDMA-related deaths are rare, they do occur. Some of the mechanisms of MDMA-related death include strokes associated with MDMA-induced hypertensive episodes, seizures, liver failure, or cardiac arrhythmias. The danger of MDMA-related death is increased if the abuser has ingested multiple compounds, or high doses of MDMA. Kalantar-Zaden, Nguyen, Chang, and Kortz (2006) discussed a case in which an otherwise healthy 20-year-old female college student, who had a history of MDMA misuse, was transported to the hospital with abnormally low blood sodium levels. In spite of aggressive medical care, she died about 12 hours after her arrival at the hospital.

Medication Interactions Involving MDMA

In the past, physicians thought that beta adrenergic blockers (β -blockers, or beta blockers) were helpful in treating MDMA toxicity, but the team of Rochester and Kirchner (1999) challenged this clinical belief on the grounds that the alpha adrenergic system would remain unaffected, and this could impact on blood pressure in spite of the use of β -blockers. The use of haloperidol was also not recommended, as the interaction between MDMA and haloperidol might interfere with body temperature regulation (Brust, 2004). The best treatment for MDMA toxicity is thought to be supportive treatment, with maintenance of normal body temperature, airway and cardiac support, and the judicious use of a benzodiazepine to control anxiety, if necessary (Schuckit, 2006a). There have been case reports of interactions between MDMA and the antiviral agent ritonavir (Concar, 1997; Harrington, Woodward, Hooton, & Horn, 1999). Each agent affects the serotonin level in the blood, and the combination of these two compounds can result in

a three-fold higher MDMA level in the blood. Some fatalities have been reported in those who have mixed these compounds (Concar, 1997).

Salvia Divinorum

Although *Salvia divinorum* has been used for generations in central Mexico and South America during religious and healing ceremonies, it is a relatively new arrival in the hallucinogenic market in this country. Media attention on the misuse of *Salvia divinorum* as the “next LSD” has helped fuel curiosity about this plant in the United States. It remains legal in some states, and may garner further restrictions in the future. Because it is a recent arrival on the drug scene, the pharmacokinetics of *Salvia divinorum* have only recently been investigated. The active agent of this plant is *salvinorin A*, which functions in the brain as kappa opioid receptor agonist⁴³ (Lehne, 2013; NIDA Info Facts, 2007), although there is evidence that it also functions as a partial dopamine D2 receptor agonist. It does not appear to have any effect on the serotonin 5-HT_{2a} receptors, where compounds such as LSD bind (MacLean et al., 2015).

The effects last for between 30 seconds and 30 minutes, depending on the potency of the leaves, and the individual's history of *Salvia divinorum* use. Individuals report experiencing dissociation and hallucinations or “visions.” An unintended effect is reduced motility in the intestines, an effect consistent with its ability to bind at the kappa opioid receptor site. One method of misuse is oral ingestion of a form of “tea” made by brewing the leaves in water, or by smoking. Other individuals will chew *Salvia divinorum* leaves. However, because salvinorin A is destroyed by gastric juices, the individual usually will hold a wad of partially chewed leaves against the gums so that the substance can be absorbed through the oral mucosa. Some individuals will attempt to inhale vapors produced when salvinorin A is heated, although this exposes the user to possible lung damage from the high temperatures involved in this process. Most users smoke the products that have been purchased via the internet or through local shops (Garcia-Romeu et al., 2016). When smoked, the effects peak within 60 seconds and 2 minutes and last for less than 20 minutes (Garcia-Romeu et al., 2016), after which the effects blend back into everyday reality within a half hour's time. The effects of this substance include laughter, revisiting memories, a sense of motion, visual disturbances, unusual thoughts, a sense of merging with objects in the environment, slurred speech, dizziness, mood swings, and dissociation.

⁴³Discussed in Chapter 14.

There have been two case reports of a persistent psychotic reaction in individuals who have used *Salvia divinorum*, although the symptomology cannot be clearly linked to the use of this substance (MacLean et al., 2015). Because it is a kappa opioid⁴⁴ agonist, its misuse potential is thought to be low, and one is hard pressed to find a reason why it is used beyond the fact that it is a novel substance.

PCP and Hallucinogen Use and the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition⁴⁵

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (American Psychiatric Association, 2013) elected to consider phencyclidine separately from the other hallucinogens, which is surprising since it is rarely intentionally misused. The *DSM-5* reviewed the diagnostic categories that might result from the use of phencyclidine or any of the other known hallucinogens and identified nine subforms of the hallucinogen-related disorders:

1. *Phencyclidine intoxication*
2. *Phencyclidine use disorder*
3. *Other phencyclidine-induced disorders*
4. *Unspecified phencyclidine-related disorder*
5. *Other hallucinogen use disorder*
6. *Other hallucinogen intoxication*
7. *Other hallucinogen-induced disorders*
8. *Hallucinogen persisting perception disorder*
9. *Unspecified hallucinogen-related disorder*

As is evident from the above list, phencyclidine is considered independently and not with the other hallucinogens. Some of the signs of a *phencyclidine use disorder* listed in the *DSM-5* include⁴⁶ (but are not limited to) (a) development of tolerance to its effects, (b) unsuccessful efforts to reduce or stop phencyclidine use, (c) craving for this compound between periods of active use, (d) spending a great deal of time in activities either directly or indirectly associated with phencyclidine use, and (e) use of phencyclidine in situations where it is physically dangerous for the individual to do so.

⁴⁴See Chapter 11.

⁴⁵The material presented here is to illustrate the relationship between the alcohol use disorders and the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition). This material should not be interpreted as, nor should it be used as, a diagnostic manual.

⁴⁶The reader is referred to the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) for a full list of the diagnostic criteria and an explanation of their meaning, should the reader be so motivated.

The symptoms of *phencyclidine intoxication* are the same as those discussed earlier in this chapter. The category *other phencyclidine-induced disorders* addresses the importance of determining whether some of the observed symptoms are caused by the concurrent use of other drugs or preexisting psychiatric disorders. *Other hallucinogen intoxication* symptoms are the same as those discussed earlier in this chapter, and include (a) dilation of the pupils, (b) tachycardia, (c) sweating, (d) heart palpitations, (e) blurred vision, (f) tremor, and (g) loss of muscle coordination. These symptoms must develop in a person who has recently ingested a hallucinogen, in a person who is fully conscious, and are not symptoms of a coexisting medical disorder.

The *DSM-5* discussion of the hallucinogens is unique in that a withdrawal syndrome is not postulated for these compounds. However, a *hallucinogen persisting perceptual disorder* category is suggested. These are the flashback phenomena reported for compounds such as MDMA and LSD discussed in this text, which cannot be explained by the presence of a concurrent medical disorder. The signs of the *other hallucinogen-induced disorders* as identified in the *DSM-5* essentially parallel those for phencyclidine. Given the similarity between the criteria for the various hallucinogen-related and phencyclidine-related conditions, further discussion of these conditions as separate categories is not carried out at this time. The reader is referred to the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (American Psychiatric Association, 2013) for a comparison of the similarities and differences between these two categories.

Chapter Summary

The phenomenon of hallucinogen misuse has waxed and waned over the years, with individuals who misuse hallucinogens rushing to embrace first one compound and then another. The compound LSD, the prototype hallucinogen, was popular in the 1960s, while phencyclidine (PCP) became popular in the 1970s and 1980s. Currently, MDMA is a popular hallucinogen to misuse. All of these compounds continue to be misused, although the trends for their use continue to change. The phenomenon of hallucinogen misuse appears to reflect a desire on the part of some people to alter their perception of reality, and possibly to achieve euphoria from the drug's effects. As we stand on the brink of molecular pharmacology, it is logical to expect that the techniques used to develop more effective pharmaceuticals will eventually be used by illicit drug manufacturers to produce even more potent hallucinogenic pharmaceuticals, ensuring that the misuse of these compounds will remain a problem well into the 21st century.



CHAPTER 13

Misuse of Inhalants and Aerosols

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 13.1** Understand the history of inhalant misuse
- 13.2** Understand the scope of the problem of inhalant misuse
- 13.3** Comprehend the pharmacology, methods of use, and subjective effects of inhalants
- 13.4** Describe the consequences of inhalant use
- 13.5** Understand the *DSM* criteria for inhalant related disorders

Introduction

The term **inhalant** does not refer to a specific compound, but to a *method of substance use* that introduces any of a wide variety of compounds into the user's body. Many such compounds are toxic, including various cleaning agents, herbicides, pesticides, gasoline, kerosene, certain forms of glue, lacquer thinner, and some of the chemicals used in felt-tipped pens. None of these compounds is intended to be introduced into the human body; however, when inhaled, each of these compounds alters normal brain function, and may induce a sense of euphoria. Adolescents in particular often discover this fact, and younger individuals learn by imitating their older siblings' behavior. Unfortunately, it is possible for children and adolescents to purchase dozens, perhaps hundreds of potential inhalants without parental permission.

Inhalant misuse is normally a time-limited phase for children and adolescents, and after a year or two they grow tired of the process and discontinue it. Many misuse an inhalant just a few times out of curiosity and then discontinue the practice. However, on occasion, the child or adolescent will continue to use inhalants, and it is not unheard of for an adult to enter treatment for inhalant use. Because these compounds are so readily available, widely misused, and have a terrible potential for harm to the individual, this chapter will focus on the problem of inhalant misuse.

A Brief History of Inhalant Use

The use of inhaled compounds to alter the user's perception of reality might be traced back at least to ancient Greece, and the Oracle at Delphi (Hernandez-Avila & Pierucci-Lagha, 2005). Historians believe that the Oracle would inhale fumes from a volcanic vent, and then, while in a state

of delirium, deliver prophetic statements that the recipient was then supposed to interpret. In the 19th century, use of the newly discovered anesthetic gasses for recreation became popular. The 20th century saw the introduction of gasoline and various industrial solvents, which quickly became compounds that were misused by inhalation (Evans et al., 2005; Hernandez-Avila & Pierucci-Lagha, 2005; Sharp & Rosenberg, 2005).

The mainstream media paid little attention to the problem of inhalant misuse until the 1950s and 1960s, when the practice of “glue sniffing” became popular (Brust, 2004). The glue used to hold model ships, planes, and automobiles together often contained the compound toluene,¹ which, when inhaled, can alter the individual’s consciousness. It is not known why the practice of glue sniffing began, but historical evidence suggests that it began in California. The first known reference to glue sniffing was in a Denver newspaper (Brust, 2004; Sharp & Rosenberg, 2005). Other newspapers began to cover the story of inhalant misuse, in the process explaining exactly how children or adolescents should use airplane glue to become intoxicated, and what effects they should expect. Although the media stories first appeared in U.S. newspapers, the problem of inhalant misuse is now recognized as a worldwide one. In many Third World countries, the use of inhalants helps to dull the individual’s awareness of hunger while achieving a sense of euphoria (Weiss, 2007). Inhalant misuse has been especially popular in Europe and Japan for recreational purposes, and, despite a downward trend in use, the problem has never entirely disappeared among young children and adolescents (Brust, 2004; Johnston, O’Malley, Miech, Backman, & Schulenberg, 2017; Karch, 2009).

The Pharmacology of the Inhalants

The inhalants are not a specific drug, but a range of compounds that share a common method of misuse. While cocaine or heroin may be “snorted,” this does not place them in the category of an inhalant, since the goal of this process is to deposit the powder in the blood-rich tissues of the sinuses, not the lungs, for absorption. A true inhalant is absorbed through the lungs and passed into the general circulation from there. Other substances that are inhaled are not classified as inhalants, as they already fit into other distinct categories (Balster, Cruz, Howard, Dell, & Cottler, 2009), and thus are covered in other chapters of this text. The compounds covered in this chapter were never intended to be used in this

manner or at the levels some inhale them, much less used for their intoxicating effects.

Inhalation is one of the most effective means to introduce a compound into the general circulation. Many molecules are able to cross over from the lungs into the circulation quickly and effectively, a trait that physicians often rely on to introduce anesthetic gases into a patient’s body to induce unconsciousness for major surgery. Those who misuse inhalants also rely on this rapid means of introducing a compound into the circulation to induce pleasure. A number of different classification systems of inhalants have been suggested, two of which are reviewed in Table 13-1.

Children and adolescents will usually misuse compounds that fall into the first two categories, but will have limited access to the third category of compounds in Espeland’s (1997) classification system. The misuse of surgical anesthetics is usually limited to health care professionals or medical school students who have access to such compounds (Hernandez-Avila & Pierucci-Lagha, 2005). None of the classification systems are perfect, but have been broadly based on categorizing by chemical classification, form of the inhalant (e.g., vapor vs. liquid), type of product (e.g., cleaner vs. adhesive), or pharmacology of the products (Balster et al., 2009). Balster and colleagues (2009) call for a better classification in the future, once research clearly identifies those substances that are pharmacologically similar and also follow similar patterns of use.

The most common inhalants are simple, carbon-based molecules such as benzene, toluene, hexane, acetone, butane, and ethyl chloride (Ricaurte, Langston, & McCann, 2008). All of these compounds, plus gasoline fumes (another favorite inhalant in some regions of the world), are able to enter the bloodstream without their chemical structure being altered in any way (Bruckner & Warren, 2003). The compounds most commonly used as inhalants are very lipid-soluble, a characteristic that allows those molecules to rapidly cross the blood-brain barrier (BBB) into the brain within seconds of their use (Crowley & Sakai, 2004a; Evans et al., 2005; Hassan, Bhatia, & Bhatia, 2017).

TABLE 13-1 Comparison of Two Inhalant Classification Systems

	Brust (2004); Crowley and Sakai (2005a)	Espeland (1997)
1	Solvents	Organic solvents
2	Propellants (used in spray cans)	Aerosols (used in spray cans)
3	Paint thinners	Volatile nitrites (amyl nitrite or butyl nitrite)
5	Fuel fumes	General anesthetic gasses

¹This compound has since been removed from model airplane glue.

Parents will often ask why, if children are misusing various compounds through inhalation, the government does not just outlaw these products. The answer to this question is that this is virtually impossible. There are hundreds (Howard, Bowen, Garland, Perron, & Baughn, 2011) or perhaps *thousands* of common household or industrial products that might be used as inhalants (Hassan et al., 2017; McGuinness, 2006; Wolfe, 2009). Further, children and adolescents are adept at finding compounds around the house that might be used as inhalants. For example, the team of Feuillet, Mallet, and Spadari (2006) presented a case history in which twin sisters were inhaling mothball fumes to become intoxicated.

The effects of an inhalant are dependent on (Wolfe, 2009) (a) the chemical(s) being used, (b) the intensity of exposure, (c) the body size of the individual, (d) the individual's expectations for the effects of that compound, (e) the setting in which the inhalant use takes place, and (f) the individual's general state of health. Given the interaction among these variables, and the wide variety of compounds that might be used as inhalants, it is impossible to speak of a class-specific "pharmacology" or "toxicology" of these compounds. The elimination half-life of different inhalants might range from hours to days, depending on the specific compound being used (Brooks, Leung, & Shannon, 1996). The half-life of most solvents is also longer in individuals who are obese, since these compounds bind to lipid molecules. Given the current epidemic of childhood obesity in the United States, this is a matter of some concern for health care professionals who work with those who misuse inhalants, since it would be expected that the molecules of the inhalant(s) would bind to the adipose cells. This is, however, an assumption that needs further research, as only recently have these substances gained research attention (Crossin, Cairney, Lawrence, & Duncan, 2016; Duncan & Lawrence, 2013; Howard et al., 2011).

Many of the commonly misused inhalants do share some common toxicological characteristics, one of which is that many of these compounds must be biotransformed by the liver before the process of elimination (usually by the kidneys) can begin (Bruckner & Warren, 2003). There are exceptions to this rule, however: The anesthetic gasses are exhaled without extensive, or in some cases any, biotransformation taking place (Crowley & Sakai, 2004a). Because the pharmacokinetics of an inhalant varies from one compound to the next, little information is available about the effects of individual compounds at the cellular level (Haut, Moran, & Lonser, 2012; McGuinness, 2006; Virani, Bezchlibnyk-Butler, & Jeffries, 2009). Even where such research has been conducted on these substances, individuals who have been misusing inhalants often use concentrations of the compound(s) of choice that are

orders of magnitude beyond those that are used in the research (Bruckner & Warren, 2003). To illustrate this point, consider that the safe exposure level for toluene fumes in the workplace is 10–100 parts per million (ppm), with the danger level to life and health at 500 ppm (Cruz, Rivera-Garcia, & Woodward, 2014). The concentration used by those who misuse this compound through inhalation is often 50–100 times as high as the maximum permitted industrial exposure level. To further complicate matters, the individual might use a compound in which the desired substance is a secondary ingredient, exposing themselves to the effects of the primary compound in the product as well as the desired substance (Hernandez-Avila & Pierucci-Lagha, 2005).

Scientists are only recently beginning to understand the mechanism(s) by which the inhalants alter the normal function of the brain (Bowen, Howard, & Garland, 2016; Duncan & Lawrence, 2013; Evans et al., 2005; McGuinness, 2006). As a group, the compounds used by inhalation are thought to alter the normal function of the gamma-amino-butyric acid (GABA) and/or N-methyl-D-aspartate (NMDA) (Crowley & Sakai, 2004a; Duncan & Lawrence, 2014). Behavioral observations on animals exposed to an inhalant suggest that their effects are similar to those of alcohol or the barbiturates, which is consistent with neurological data suggesting that all of these compounds bind at the same gated ion channel in the neural cell wall. It has been observed that some inhalants potentiate the effects of CNS depressant use, such as alcohol and the benzodiazepines,² possibly with fatal results. As should be apparent by now, more investigation into the pharmacological effects of these compounds is needed, and their effects can be influenced by so many different factors that there is no standard pharmacology of the inhalants.

Scope of the Problem of Inhalant Misuse

Inhalant misuse is a worldwide problem, a fact that is often overlooked by the mass media in this country. Approximately 9% of the population of the United States has misused an inhalant at least once (Howard et al., 2011; SAMHSA, 2016). This is consistent with the observation that 5% of high school seniors in 2016 admitted to the use of an inhalant at least once (Johnston et al., 2017). It has been estimated that 9.1% of adolescents age 12–17 misused an inhalant at least one time in 2015, 2.7% misused an

²The reader is reminded that any known or suspected overdose should immediately be assessed by a physician.

inhalant in the past 12 months of when surveyed, and 0.7% have indicated misuse of an inhalant in the past month (SAMHSA, 2016). Brust (2004) suggested that boys were more likely to misuse inhalants than girls by a ratio of 10:1, while Spiller and Krenzelok (1997) suggested that the ratio was 3:1.

It is frightening to note that many who misuse these compounds do not view this as a form of “drug” misuse (Wolfe, 2009) and do not see the risks (Johnston et al., 2017). Inhalant misuse, for the most part, is limited to experimental use that occurs a few times and then is discontinued, without the child or adolescent going on to develop other drug problems (Crowley & Sakai, 2005a; Howard et al., 2011). However, on occasion the individual does become physically dependent on an inhalant. The mean age at which individuals begin substance-centered inhalation is about 13 years (Anderson & Loomis, 2003; Marsolek, White, & Litovitz, 2010). For the most part, inhalant misuse is an episodic phenomenon during the teen years, after which point most adolescents mature out of this practice (Evans et al., 2005; Hassan et al., 2017; Marsolek et al., 2010). There are reports of children as young as 3 years of age misusing inhalants, however, and so it is important to keep in mind the fact that young children do misuse inhalants on occasion (Crowley & Sakai, 2005a). Individuals with an inhalant misuse problem are usually not referred to a rehabilitation facility until the individual is over the age of 18 (SAMHSA, 2011a).

It has been estimated that only about 4% of individuals misusing inhalants become addicted to a compound misused through inhalation (Brust, 2004). Hernandez-Avila and Pierucci-Lagha (2005) identified four patterns of inhalant abuse:

1. *Transient social use* occurs for a brief period of time in response to social situations, usually involving individuals 10–16 years of age.
2. *Chronic social use.* The individual misuses an inhalant for 5 or more years with others, usually seen in individuals 20–30 years of age. These individuals demonstrate signs of brain damage, and usually have minor legal problems in their histories.
3. *Transient isolated use.* A short history of solo inhalant misuse by individuals, usually 10–16 years of age.
4. *Chronic isolated use.* A history of continuous solo misuse of inhalants lasting for 5+ years, with a history of serious legal problems and possible evidence of brain damage.

There is lively debate over whether inhalants serve as a “gateway” to further drug misuse. It has been found, for example, that 23% of individuals who use cocaine had a history

of prior inhalant misuse (Worchester, 2006). It has been found that people who admit to a history of inhalant misuse were 45 times more likely to engage in the practice of self-injected drug use, while those individuals who admit to the use of inhalants *and* marijuana use were 89 times as likely to have used injected drugs, as compared to the general population (Crowley & Sakai, 2005a). These figures, while disturbing, raise an interesting question: Does the inhalant misuse pave the way for further drug misuse, or do those persons who are more likely to misuse drugs begin with inhalant misuse and then “graduate” to other forms of substance use later in life? This debate has not been resolved, and the debate over whether inhalants serve as a gateway to later drug misuse continues.

Methods of Inhalant Misuse

There are a number of ways that inhalants might be misused, and the specific method of use is dependent on the specific compound being misused (Anderson & Loomis, 2003; Wolfe, 2009). Some compounds may be inhaled directly from their container, a practice called **sniffing** or **snorting**. Helium is often used in balloons and is often used in this manner, as is nitrous oxide (Northcutt, 2008; Stockton, Simonsen, & Seago, 2017). Other compounds are poured into a plastic bag, which is then placed over the individual's mouth and nose, so that the individual can inhale concentrated fumes, a practice called **bagging** (Anderson & Loomis, 2003; Nelson, 2000). Still other compounds are poured onto a rag, which is then placed over the individual's mouth and nose, called **huffing**, which allows the fumes to be inhaled along with air (Anderson & Loomis, 2003; Nelson, 2000).

Fumes from aerosol cans may be directly inhaled or sprayed into the mouth. An example of those fumes that are directly inhaled is cigarette lighters. Individuals will activate the cigarette lighter without lighting it, allowing the fumes to escape the container for inhalation. Finally, there are those compounds that might be heated, releasing the fumes, which are then inhaled (Nelson, 2000). Obviously, if the compound being misused should be flammable, there is a significant risk of fire should the compound being heated be exposed to an open flame or a spark, but this is a risk that individuals using these compounds either are not aware of or dismiss as a cost of their misuse of inhalants.

Subjective Effects of Inhalants

The initial effects of an inhalant begin within seconds to, at most, minutes, and last for approximately 45 minutes per episode of misuse (Schuckit, 2006a; Zevin & Benowitz,

TABLE 13-2 Desired Effects of Inhalant Abuse

Alcohol-like euphoria and sense of intoxication
Altered voice (when substances such as helium are abused)
Altered state of awareness
Hallucinations
Fantasies (some vivid)
Feelings of invincibility
Loss of inhibitions
Numbness
Sense of spinning around

NOTE: Effects differ based on substance(s) misused.

2007). The desired effects from inhalants include those listed in Table 13-2 (Anderson & Loomis, 2003; Brust, 2004; Sharp & Rosenberg, 2005; Virani et al., 2009; Wolfe, 2009; Zevin & Benowitz, 2007):

Complications Induced by Inhalant Misuse

When inhalant misuse first emerged in the 1950s and 1960s, most health care professionals did not think there were any serious health consequences associated with the practice. This is no longer assumed to be true. In the last quarter of the 20th century, scientists concluded that, depending on (a) the substance being misused, (b) the method of misuse, (c) the level of substance exposure, and (d) the frequency of misuse, the individual might experience significant health problems, and possibly death (Worchester, 2006). The duration and intensity of exposure are important variables that cannot be quantified: In the industrial setting, a worker might be exposed to high levels of one or more compound in an isolated incident, whereas an individual misusing inhalants might be exposed to far higher levels each time the same compound is misused.

A partial list of potential consequences from inhalant misuse includes those listed in Table 13-3 (Anderson & Loomis, 2003; Brust, 2004; Crossin et al., 2016; Crowley & Sakai, 2004, 2005a; Han, Goforcer, & Colliver, 2010; Haut et al., 2012; Howard et al., 2011; Joshi, Sapkota, & Sharma, 2017; Karch, 2009; Lezak, Howieson, Bingler, & Tranel, 2012; Sharp & Rosenberg, 2005; Stockton et al., 2017; Virani, Bezchlibnyk-Butler, Jeffries, & Procyshyn, 2012; Weiss, 2007; Wolfe, 2009; Worchester, 2006; Zevin & Benowitz, 2007).

Approximately 50% of deaths attributed to inhalant misuse are the result of inhalant-induced ventricular

TABLE 13-3 Possible Health Consequences of Inhalant Misuse

Cardiopulmonary System
Anoxia and/or respiratory depression, possibly to point of death
Aspiration of vomited material (may result in death, especially if abuser is unconscious)
Bone marrow damage resulting in reduction in red blood cell production
Cardiac arrhythmias such as ventricular fibrillation (may prove fatal)
Cough/wheezing
Erosion of nasal mucosa, formation of ulcers in nose, mouth, and throat
Exacerbation of asthma or similar disorders
Lung function changes, possible chronic lung disease/infections
Sinusitis (irritation of sinus tissues; may become permanent)
Tuberculosis (increased vulnerability toward development of)
Central Nervous System
Cerebellar ataxia
Deafness, or loss of hearing (may become permanent)
Encephalopathy
Nystagmus
Organic brain damage (including possible drug-induced dementia)
Peripheral neuropathies
Seizures
Tremor (may become permanent)
Visual impairment (may become permanent)
Polyneuropathy
Psychiatric
Anxiety
Confusion
Depression
Mania
Psychological dependence on further inhalant (or drug) use
Psychosis (drug-induced) (may become permanent)
Other Complications
Chemical burns to skin, especially around mouth/nose
Kidney damage (might be permanent)
Laryngitis
Light sensitivity
Liver damage (possibly permanent)
Muscle tissue damage secondary to rhabdomyolysis
Vomiting, possibly leading to aspiration-induced death
Severe vitamin B12 deficiency
Failure to thrive in children and adolescents

fibrillation³ or **sniffing death syndrome** (McGuinness, 2006). Such deaths can occur the first time an individual misuses an inhalant, or the 200th time (Collins, 2004). Further, depending on the substance being misused, the individual might introduce various heavy metals such as copper or lead into his or her body, which will have lifelong consequences (Crowley & Sakai, 2005a; Lezak et al., 2012). Lead was once an additive to gasoline and many forms of paint in the United States and was a common cause of lead poisoning when it was misused as an inhalant. Lead has been removed from gasoline in the United States, and thus lead poisoning is not a significant risk, but there are still a handful of countries that have leaded gasoline. If the compound being misused is a propellant-packaged substance (spray cans of paint, for example), the individual runs the risk of coating the inside of the lungs with the compound itself, although the propellant was the desired substance to be misused. This may interfere with the normal function of the lungs, if not block it entirely, resulting in the individual's death.

Although a standard neurological examination is often unable to detect solvent-induced organic brain damage until it is relatively advanced, sensitive neuropsychological tests often detect signs of inhalant-induced brain damage even in industrial workers who are exposed to levels far lower than those utilized by those misusing inhalants. Toluene is a prime example of this, and chronic toluene exposure can induce intellectual impairment, as well as leukoencephalopathy and atrophy of the optic nerves (Crowley & Sakai, 2004, 2005; Ricaurte, Langston, & McCann, 2008).

Upon the cessation of an episode of inhalant misuse, the individual will go through a withdrawal syndrome that, at its extreme, can be similar to alcohol-induced delirium tremens (DTs) (Hernandez-Avila & Pierucci-Lagha, 2005). The exact withdrawal syndrome will depend in large part on the exact compound(s) being misused, the length of exposure, the concentration of the compound(s) used, and any possible concurrent substance misuse. Some of the withdrawal symptoms observed during severe inhalant withdrawal include muscle tremors, irritability, anxiety, insomnia, muscle cramps, hallucinations, sweating, nausea, a foul odor on the individual's breath, loss of vision, and possible seizures (Crowley, 2007; Hassan et al., 2017; Worchester, 2006).

Inhalant Misuse and Suicide

There is a strong correlation between inhalant misuse, depression, and suicidal behavior (McGuinness, 2006). Since depression is a risk factor for suicidal behavior, and depression is a common consequence of inhalant misuse, there is a

potential for suicidal behavior following episodes of inhalant misuse. The more intense the frequency and duration of inhalant misuse, the greater the risk for suicidal behavior (Espeland, 1997; Freedenthal, Vaughn, Jenson, & Howard, 2007). Unfortunately, when death does occur, it is often difficult to determine whether the individual intended to end his/her life or not. Some of the methods of inhalant misuse lend themselves to ambiguity as to whether death was intentional or accidental. For example, if the individual inserts his or her head into a plastic bag after filling the bag with inhalant fumes and then closes the bag around the head and neck before beginning to inhale the fumes, it is difficult to determine whether the individual's death was an actual suicide or not, unless the individual left behind a suicide note (Espeland, 1999). However, intentional or unintentional death is a very real danger when an individual misuses an inhalant.

Anesthetic Misuse

The first two anesthetics used, nitrous oxide and ether, were first recreational substances (Hernandez-Avila & Pierucci-Lagha, 2005). Their potential as surgical anesthetics were only recognized when Horace Wells attended a party in which people were indulging in nitrous oxide misuse and observed a person under its influence injure himself without apparent pain. Unfortunately, the first planned exhibition of nitrous oxide as a surgical anesthetic agent was something less than a success.⁴ This did not prevent some intrepid explorers from examining the effectiveness of various compounds as potential surgical anesthetics, and with some success. The pharmacological effects of general anesthetics are similar to those induced by the barbiturates (Hernandez-Avila & Pierucci-Lagha, 2005). There is a dose-dependent response ranging from sedation through sleep, and, as the dose increases, to analgesia, unconsciousness, and, in extreme cases, death. Although medical school students will occasionally misuse compounds such as ether, chloroform, trichloroethylene, and halothane, the most commonly misused anesthetic gas is nitrous oxide, which we will examine in more detail below.

Nitrous Oxide

The surgical anesthetic gasses are able to induce a loss of consciousness, during which the patient is less responsive to painful stimuli. The question of whether the person can still

³A cardiac arrhythmia.

⁴At the time, it was not recognized that nitrous oxide has a short duration of action when used as a surgical anesthetic. The patient woke up in the middle of the operation, screaming in pain. The proper use of nitrous oxide as a surgical anesthetic was not discovered until several years after this inauspicious beginning.

perceive pain or not has been debated, especially with the discovery that patients under anesthesia can apparently recall some things said in the surgical theatre while they were supposedly unconscious. This raises the question whether the surgical anesthetics block the individual's awareness of the pain or just make them less responsive to the pain they experience, a topic that is being explored through research at this time.

Nitrous oxide blocks the glutamate neurotransmitter molecules from the NMDA receptor sites. Since glutamate is the main excitatory neurotransmitter in the brain, it becomes clear why this substance is able to function as an anesthetic gas. It also reduces the effectiveness of acetylcholine as a neurotransmitter, which contributes to the reduction in the individual's level of consciousness (Lewis, 2011). However, to prevent the risk of death by **hypoxia**,⁵ the physician (or dentist, since it is often used during dental surgery) must supply oxygen at **over pressure**⁶ during the procedure. Individuals often do not know about this characteristic of nitrous oxide, and very few have access to the equipment necessary to supply oxygen at over-pressure. Thus, those misusing nitrous oxide run a substantial risk of hypoxia-induced brain damage or even death while using this substance.⁷

In low doses, those misusing nitrous oxide report feelings of euphoria, giddiness, hallucinations, and a loss of inhibitions. At higher doses, there is a loss of consciousness, and possible death at extremely high doses. The volatile anesthetics are not extensively biotransformed by the body, but enter and leave the body virtually unchanged. Once the source of the anesthetic is removed, such as when a surgical procedure is completed, the concentration of the anesthetic in the brain will begin to drop, and eventually the patient is able to regain consciousness and begin the process of recovery.

The Misuse of Nitrites

There are different forms of nitrites commonly misused: (1) the pharmaceutical compound amyl nitrite, which is used in certain heart conditions, (2) butyl nitrite, and (3) isobutyl nitrite. While inhaled, all of these compounds function as coronary vasodilators, allowing more blood to flow to the heart. This is why amyl nitrite is used in the control of angina pectoris: When administered, it allows the coronary arteries to dilate for a short time, increasing the blood flow to the heart. Amyl nitrite is administered in small glass containers embedded in layers of cloth. When needed, the

user will “snap” or “pop”⁸ the container in his or her fingers, and inhale the fumes to achieve the desired effect.

With the introduction of nitroglycerin preparations, which are as effective as amyl nitrite but lack many of its disadvantages, amyl nitrite has fallen into disfavor and is now only rarely utilized (Hernandez-Avila & Pierucci-Lagha, 2005). Still, it does have a limited role in medicine, such as in certain diagnostic procedures and the treatment of cyanide poisoning. Individuals who misuse nitrite prize these amyl nitrite capsules, using them in much the same manner that they misuse butyl nitrite or isobutyl nitrite. These latter compounds are available by mail order houses, on the internet, or in specialty stores, depending on state regulations for the specific area. In many areas, butyl nitrite is sold in small bottles as a “room deodorizer.” Many individuals who misuse this substance believe that butyl nitrite will induce a prolonged orgasm if inhaled just before the individual achieves this state.⁹

Since amyl nitrite is known to induce delayed orgasm and impotence in male users, it is not unreasonable to expect that its close chemical cousins would also induce these effects. The aftereffects of the use of these compounds include an intense, sudden headache, increased pressure in the fluid in the eyes (a danger for patients with glaucoma), possible weakness, nausea, retinal damage, and cerebral hemorrhage induced by nitrite-induced increased blood pressure (Audo, Sahel, & Paques, 2010; Karch, 2009). In addition, the nitrites appear to suppress the action of the body's immune system, especially the natural killer cells, possibly increasing the user's risk for infection after using nitrites. Individuals who misuse these substances are willing to run the risk of these adverse events, though most people wonder why a person would be willing to run these risks for just a few seconds of perceived pleasure.

Inhalant Misuse and the *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition

The Diagnostic and Statistical Manual of Mental Disorders (5th edition) (DSM-5) (American Psychiatric Association, 2013) identified four subforms of the inhalant-related disorders:

- Inhalant use disorder
- Inhalant intoxication

⁵See Glossary.

⁶See Glossary.

⁷This is a risk inherent in the use of many anesthetic gasses, but this lies outside of the scope of this textbook.

⁸Thus, the name used by illicit users of “poppers” or “snappers.”

⁹The author of this text has met individuals who misuse butyl nitrite and who claim that rather than enhance sexual pleasure, butyl nitrite actually interfered with their enjoyment of the sexual encounter.

- Other inhalant-induced disorders
- Unspecified inhalant-related disorder

The *inhalant use disorder* is equivalent to inhalant addiction, a phenomenon that resembles alcohol intoxication. The *DSM-5* warned that those who misuse inhalants often use several compounds simultaneously, making the differential diagnosis difficult. The *DSM-5* suggested that *inhalant intoxication* be considered when the individual demonstrates any of the criteria for intoxication outlined in this chapter without evidence of concurrent misuse of other compounds such as alcohol. One diagnostic sign for inhalant intoxication is the smell of the compound(s) being misused on the individual's breath or the possession of compounds primarily used for intoxicating purposes.

Only about 10% of individuals misusing inhalants develop a tolerance to their compound of choice (American Psychiatric Association, 2013). Children with either a conduct disorder or an antisocial personality disorder appear to be at greater risk for inhalant misuse or addiction (American Psychiatric Association, 2013), although other personality types are also vulnerable to the lures of inhalant misuse. The condition *other inhalant-induced disorders* refers to psychiatric conditions caused or exacerbated by the misuse of inhalants, whereas the *unspecified inhalant-related disorder* refers to those cases in which the individual has developed social, occupational, familial, or other symptoms of an inhalant use disorder, but who do not meet the full criteria for this condition (American Psychiatric Association, 2013). For

each of these conditions, modifiers, such as in early or in sustained remission, as well as whether the individual is in a controlled environment where access to such compounds is limited, may be applied as appropriate in the assessor's opinion.

Chapter Summary

Inhalant misuse appears to be a phase through which some children and adolescents pass. For the most part, the individual engages in a few episodes of inhalant misuse over a period of 1–2 years, and then discontinues the practice. However, a small percentage of individuals go on to misuse other compounds, and an even smaller percentage of individuals continue to use inhalants for extended periods. The effects of these compounds are short-lived, although this depends on the specific compound(s) being used, and the intensity with which the individual inhales the compound(s). Since there are literally thousands of commercial products that may be misused as inhalants, these compounds are easily available to children and adolescents, and thus may contribute to their attractiveness as drugs of misuse. However, inhalant misuse also exposes the individual to compounds the effects of which are unknown to toxicologists, or in dosage levels that have not been studied by toxicologists. Death, or organic damage to various body organs, is possible from inhalant misuse, making these compounds a dangerous “high” for anyone.



CHAPTER 14

The Under-Recognized Problem of Steroid Misuse

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 14.1** Understand the medical uses of anabolic steroids
- 14.2** Understand the scope of the problem of anabolic steroid misuse
- 14.3** Comprehend the pharmacology and methods of use of anabolic steroids
- 14.4** Describe the hazards of anabolic steroid misuse
- 14.5** Understand how anabolic steroid-related disorders are addressed in the *DSM*

Introduction

The term “performance-enhancing” compounds has frequently been in the news as blood or urine samples from one athlete or another has revealed evidence suggesting their use by athletes seeking a competitive edge. In at least one country there have been government-supervised programs to guide the development and use of performance-enhancing drugs for its top athletes while leading the World Anti-Doping Agency to believe otherwise (McLaren, 2016), although certainly some do not agree with the accusations and evidence (Sterling, 2017). However, the use of performance-enhancing compounds is not a recent phenomenon: Greek warriors ingested deer muscle meat, or consumed special drinks and potions on the theory that this would increase their speed and endurance, and lion heart muscle on the theory that this would increase the athlete’s bravery (Aschwanden, 2012; Stephens, 2008). The gladiators of ancient Rome used a wide variety of potions in hopes of being able to gain a competitive edge over their opponents (Botre & Pavan, 2008). It is not known how effective these compounds were, but the users believed in them, which may have enhanced their fighting or athletic ability, if only through the placebo effect.

In the present era, there are a wide range of substances, including the anabolic steroids, that are misused by world-class amateur and professional athletes to enhance their own athletic performance or at least to offset any advantage their opponent might gain from using such compounds. The potential dangers associated with the use of such compounds are minimized

or ignored by these individuals, who seek to either gain an advantage over the opposition or “level the playing field”¹ should their opponent be using such compounds. On rare occasions, some individuals using these compounds desire the sense of mild euphoria induced by performance-enhancing substances. However, the major motivating factor is the desire to improve athletic performance at the local, national, and world levels.

In a sense, anabolic steroid misuse reflects two different social diseases. The first is the emphasis on appearances. This is perhaps most clearly illustrated by the trend for advertisers to describe their products as being “on steroids,” giving the impression of enhanced speed, durability, and attractiveness inherent in the use of such compounds (Pope & Brower, 2008; Rylkova, Bruijnzeel, & Gold, 2007). A percentage of the population has come to believe that the risks of anabolic steroid use are worth it to enhance their physical appearance, with 80% of individuals using steroids being men who are not competitive athletes but are focused on physical enhancement (Christou et al., 2017). The second expression of this social disease is the belief that it is acceptable to “win at any cost,” even if this involves the use of illegal and potentially lethal compounds. Many athletes will look for something—anything—that will give them a perceived “edge” over the competition. For example, Aschwanden (2012) spoke of a case where the U.S. Anti-Doping Agency suspended a teenaged in-line skater because performance-enhancing drugs had been detected in the athlete’s urine. Subsequent investigation revealed that the father of the athlete in question had been injecting him with a combination of growth hormone and steroids since the skater was 12 years old, apparently to give his son an advantage over the competition.

It would not be unreasonable to say that a “fierce competition” (Aschwanden, 2012, p. 56) has developed between those who use performance-enhancing compounds, a category that includes the anabolic steroids, and scientists who strive to develop tests that will detect the latest performance-enhancing compounds. An “arms race mentality” (Joyner, 2004, p. 81) has evolved in both amateur

and professional athletics,² in which individuals begin to use performance-enhancing compounds to overcome what they perceive to be an unfair advantage that such compounds offer the opposition. To meet the demands of both those who wish to enhance athletic performance and those who wish to improve their appearance, an acquisition and distribution network has evolved. Because of the widespread use of these compounds, it can be assumed that some it is of value for the professional within the field of addictions to have a working knowledge of these compounds and their effects.

An Introduction to the Anabolic-Androgenic Steroids

The term *anabolic* refers to the ability of these compounds to increase the speed of tissue growth or repair, possibly through the retention of nitrogen molecules within muscle tissue. The term *steroid* refers to the fact that these compounds are structurally similar to testosterone, the primary male sex hormone. Because of their chemical similarity to testosterone, steroids have a masculinizing (androgenic) effect on the user (Pope & Brower, 2008). This natural effect is seen when boys reach puberty and their bodies start to produce significant amounts of testosterone: Suddenly, muscle growth and secondary sex characteristics emerge. Although the adolescent may have been exercising prior to the onset of puberty, it is only after puberty that their efforts result in significant muscle growth. It is for this reason that the anabolic steroids are sometimes referred to as the *anabolic-androgenic steroids*³ (Lukas, 2014).

In humans, normal testosterone levels are associated with lower total cholesterol levels, lower fat mass, smaller waist circumference, and a reduction in the pro-inflammatory cytokines associated with atherosclerosis, the metabolic syndrome that often precedes the development of diabetes and the onset of diabetes itself. The problems associated with excessive levels of anabolic steroids will be discussed later in this chapter.

²Aschwanden (2012) reported that the World Anti-Doping Agency tested about half of the 14,000 athletes participating in the 2012 Summer Olympic Games. All of the medal winners were tested, as were a number of other athletes on a random basis. Tests were also conducted on blood or urine samples collected from past Olympic Games to determine whether there was evidence of use of performance-enhancing compounds that could not be identified by the technology of that era.

³For purposes of this chapter, the terms “steroids” or “anabolic steroids” will usually be used.

¹Rylkova, Bruijnzeel, and Gold (2007) estimated that up to 95% of professional football players and 80–99% of other professional athletes use anabolic steroids to enhance performance.

Medical Uses of Anabolic Steroids

Although the anabolic steroids have been in use since the 1950s, there are few approved uses for these compounds (Pope & Brower, 2005, 2008; Pope & Kanayama, 2015). Physicians will prescribe corticosteroids, close chemical cousins to the anabolic steroids, to suppress the immune system and/or inflammation as an adjunct to the treatment of various conditions. This is an important distinction for the reader to keep in mind. Anabolic steroids are occasionally used to treat delayed puberty in adolescents and as an adjunct to the treatment of certain forms of breast cancer (Giri et al., 2017; Lukas, 2014). They promote the growth of bone tissue following injuries in certain cases, and might be useful in the treatment of osteoporosis (Congeni & Miller, 2002; Farooqi, van den Berg, Cameron, & Crotty, 2014; Maggio & Cimaz, 2017). Anabolic steroids might be of value in treating AIDS-related tissue loss, but beyond this there are few other legitimate applications for the anabolic steroids at this time.

Why Steroids Are Misused

As the information in the last section would suggest, there are few approved applications for anabolic steroids. Because the anabolic steroids can (1) increase lean muscle mass, (2) increase muscle strength, and (3) reduce the period of recovery time necessary between exercise periods, athletes are often drawn to them (Karch, 2009; Pope & Brower, 2008; Pope & Kanayama, 2015). They also induce a sense of euphoria in some users (Eisenberg & Galloway, 2005; Hildebrandt, Langenbucher, Carr, Sanjuan, & Park, 2006). In contrast to alcohol or the other drugs, where euphoria is the motivating factor for the substance use, those who use anabolic steroids most often seek improved athletic performance or physical enhancement through these compounds, especially if the steroid use is undetected by urine or blood toxicology testing.

Once the cycle of steroid use is initiated, many individuals continue because they develop a state of “reverse anorexia nervosa” or *muscle dysmorphia* (Kanayama, Barry, Hudson, & Harrison, 2006, p. 697; Lukas, 2014; Pope & Kanayama, 2015; Pope, Khalsa, & Bhasin, 2017). The individuals with this condition, which is more descriptive than a diagnostic category, become obsessed with their body image and fear that they might look “small” to others. This body image disorder is usually seen after the individual has been misusing anabolic steroids for an extended time, and frequently functions as an incentive for further steroid use. In many cases, the body image disorder predates the initiation of steroid use (Kanayama et al., 2006) and might explain why non-athletes who use steroids believe that these compounds will help them look

more attractive (Kanayama et al., 2006; Pope, 2010; Pope & Brower, 2008). This subgroup of individuals using steroids includes a small percentage of adolescent girls who believe that these compounds will help them lose body fat and help them look more “toned” or attractive (“Girls are abusing steroids too,” 2005), although there is concern that these results have been inflated by research methods (Pope & Kanayama, 2015).

Another subgroup of individuals who use steroids is composed of law enforcement and security officers, who believe that these compounds will increase their strength and aggressiveness (Eisenberg & Galloway, 2005; Galloway, 1997). These individuals hope that their use of steroids will give them an advantage when confronting potential law-breakers. However, many individuals misusing steroids are athletes who hope that these compounds will enhance their athletic performance. Thus, there is no “standard” individual using steroids, but various subgroups who share the characteristic of anabolic steroid use in common.

The Legal Status of Anabolic Steroids

In the United States, anabolic steroids have been classified as a Category III controlled substance⁴ since 1990. At least 59 different compounds have been identified as anabolic steroids by law enforcement officials, and their use for non-medical purposes, or their sale by individuals not licensed to possess and distribute them, is a crime punishable by a prison term of up to 5 years (10 years if the steroids are sold to minors). The most common steroids found by law enforcement include testosterone, methandrostenolone, trenbolone, and stanozolol (DEA, 2013).

Scope of the Problem of Steroid Misuse

Anabolic steroid misuse is a silent epidemic, and the true scope of the misuse of these compounds is not known (Eisenberg & Galloway, 2005; Karch, 2009). There is little information about the use of performance-enhancing compounds (including anabolic steroids) by preadolescent athletes, although there have been isolated case reports in Europe (Laure & Binsinger, 2007). In the United States, urine toxicology testing for performance-enhancing drugs in athletes does not begin until high school, and so the use of such compounds by preadolescents is possibly more widespread than suspected (Laure & Binsinger, 2007).

⁴See Appendix 3.

Johnston, O'Malley, Backman, and Schulenberg (2017) reported that 1.9% of high school seniors surveyed had misused an anabolic steroid at least once, whereas Elkins, King, Nabors, and Vidourek (2017) found that 2.6% of their sample misused an anabolic steroid in the past year. Many of those individuals who are using anabolic steroids are male athletes on the high school, college, and professional levels, although in light of the ever-growing sophistication of forensic laboratory testing for college and professional athletes, many are turning to nonsteroidal compounds to enhance muscle growth (Lukas, 2014). There is mixed evidence suggesting that steroid use among adolescent girls might be increasingly common ("Girls are abusing steroids too," 2005; Lukas, 2014); however, some discount this theory because these medications have an androgenic effect, which would be most unwelcome for the typical adolescent girl, in addition to concerns about the research methods (Pope & Brower, 2008; Pope & Kanayama, 2015). Although anabolic steroid use was seen most often in older adolescents, there is a disturbing trend for younger adolescent athletes to use these compounds, both to improve their appearance and to improve athletic ability (Calfee & Fadake, 2006; Rylkova et al., 2007).

The median age for anabolic steroid use is 18 (Karch, 2009), which is consistent with the observation that college-aged individuals using frequently report that they did not begin to use these compounds until just before or shortly after starting college (Dickensheets, 2001). Further, although the popular image of an individual misusing steroids is that of a professional athlete, Cohen, Collins, Darkes, and Gwartney (2007) found that the typical male using steroids in their research sample was a well-educated, Caucasian, 30-year-old who held a "white collar" job. Thus, although the anabolic steroids have a reputation as being misused mainly by professional athletes, in reality, steroid misuse permeates well beyond athletes, although most physicians and mental health professionals frequently overlook the possibility of their use in their assessment.

Pharmacology of Anabolic-Androgenic Steroids

The anabolic steroids are members of a group of compounds that are similar to the testosterone molecule. The basic testosterone molecule, of which there are at least 1,000 known derivatives, lends itself to a variety of functions: progesterone regulation in women, formation of adrenocortical hormones, bile acids, poisons produced by various toads, and some carcinogenic compounds. During gestation testosterone plays a role in the differentiation of the sexes, especially during the third and fourth months of prenatal development, and is involved in the prenatal development of the hypothalamus in

males. Following birth, especially after the onset of puberty, endogenous testosterone molecules reduce pain sensitivity and anxiety levels as well as motivating men to seek a sexual partner. These molecules are also involved in the formation of muscle mass following the onset of puberty, sperm production in adolescent boys, and bone maturation in both sexes.

A little-known fact is that women's bodies produce small amounts of testosterone, which is involved in the regulation of sexual arousal as well as the pair bonding process in women. For both sexes, endogenous testosterone is involved in a number of body system regulation activities.⁵ It is thought that the steroids force the body to increase cellular protein synthesis through the retention of nitrogen molecules in the cell wall. The anabolic steroids also inhibit the action of a group of chemicals known as the glucocorticoids, which cause tissue breakdown (Casavant, Blake, Griffith, Yates, & Copley, 2007; Congeni & Miller, 2002; Rylkova et al., 2007). The mechanism by which this is accomplished is not known, but it appears to explain why anabolic steroids are able to counteract the effects of strenuous physical exercise, contribute to the development or retention of muscle tissue, and aid in developing physical endurance. It has been hypothesized that in the brain the endogenous steroid molecules modulate the action of the GABA_A receptor, altering the user's emotions, since the GABA_A receptor is found in the brain regions involved in the aggression response, anxiety, and reproduction (Rylkova et al., 2007).

The artificial anabolic steroids might be broken down into subgroups: (1) those compounds that are active when administered orally, (2) those compounds that must be injected into muscle tissue to become active, and (3) those compounds that are delivered transdermally, through a gel or patch. The orally administered steroids are easier to take, but have a shorter half-life, are prone to biotransformation through the first-pass metabolism effect, and are more toxic to the liver than steroids administered parenterally. Those who use steroids often combine oral and injected versions (Osta et al., 2016). As will be discussed later in this chapter, individuals misusing steroids have been found to experience a wide range of behavioral problems, suggesting that the substances cross the blood-brain barrier and bind at some of the same endogenous steroid receptor sites used by endogenous testosterone molecules. However, the artificial anabolic steroid molecules are somewhat more powerful than the endogenous testosterone molecules, displacing the endogenous compounds from their receptor sites.

⁵Which lie outside of the scope of this text. If the reader is interested in learning more about the role that endogenous testosterone plays in body system regulation, he or she is referred to a good textbook on neuro-hormones and their role in the maturation and regulation of the body.

Sources and Methods of Steroid Misuse

Because anabolic steroids have few recognized medical uses, and strict controls are in place to limit the amounts prescribed by physicians, most anabolic steroids used in the United States are obtained from illicit sources (Eisenberg & Galloway, 2005), usually from outside the United States (DEA, 2013). These sources include legitimate pharmaceuticals that are diverted to the illicit market, steroids intended for the veterinary market, semi-legal compounds manufactured by illicit drug producers, and compounds smuggled into the country by a variety of means. “Internet” pharmacies are an increasingly popular source of anabolic steroids in the United States, this being the most used method of purchasing and selling steroids (DEA, 2013). Anabolic steroids might also be purchased in other countries and then smuggled into the United States. These compounds then move through an informal distribution network, often involving patrons of health clubs or gyms (Eisenberg & Galloway, 2005; Karch, 2009; Mahoney, 2006).

A number of increasingly sophisticated “rogue chemists” (Piore, 2012, p. 39) have learned to search through professional research journals, legal databases, and copyright registries to find compounds that have been classified as controlled substances by the Drug Enforcement Administration. Such rogue chemists exist in both the United States and in other countries, such as China, where their skills are highly sought after for creation of designer drugs (discussed further in Chapter 37), including steroids. They seek to modify the chemical structure of existing compounds so that they technically become “new” and therefore noncontrolled chemicals. Unfortunately, the toxicology of these new steroid-like compounds has never been determined, and even simple mistakes in their production might potentially have devastating consequences for the user. Greater control of these designer compounds was initiated through the Designer Anabolic Steroid Control Act (2014), which created tighter controls on the substances that had been identified, as well as penalties against those who falsely label such products.

In the world of professional athletics, there is also a thriving market for these designer steroids (Knight, 2003, p. 114). These substances are steroid compounds that are manufactured in secret, and supposedly undetectable by the current generation of urine or blood toxicology tests. One such example of a “designer” steroid is the compound tetrahydrogestrinone (THG). This compound was reported to have “all the hallmarks of an anabolic steroid, crafted to escape detection in urine analysis tests” (Kondro, 2003, p. 1466). THG was not detectable by urine toxicology tests until a

new test was developed for it in 2003, at which time there was a flurry of reports that THG was found in the urine of a number of athletes (“Athletes caught using a new steroid—THG,” 2003; Knight, 2003). The development of tests to detect new designer steroids is a continuing battle in an ongoing arms race between those who wish to misuse these compounds and those who wish to detect their misuse. Those who misuse steroids have also developed their own language for steroid misuse, which is summarized in Table 14-1.

TABLE 14-1 Terminology Used by Steroid Abusers

Term	Definition
Blast and cruise	Periods of alternating high and low doses of steroids. Periods of high levels of steroid use is referred to as the “blast” phase and periods of low steroid use as the “cruise” period of steroid use.
Blending	Mixing different steroids for use at the same time. This might involve both oral and injected forms of steroids.
Blitz cycles	Rapid cycles of high alternating with low levels of steroid use in attempt to avoid developing tolerance to steroid(s) being misused.
Bulking up	Increasing muscle mass through steroid use and exercise. Steroids are self-administered on a fixed schedule, with the individual also using a special diet along with anabolic steroids.
Cycling	Taking multiple doses of steroid(s) over time, with drug-free holidays intermixed with periods of active steroid use.
Doping	Using any of a range of compounds to improve athletic performance.
Injectables	Steroids designed for intramuscular injection(s).
Mega-dosing	Taking massive doses (possibly by <i>blending</i>).
Off cycle	Period when individual is abstaining from steroid use.
On cycle(s)	Period of time when individual is “cycling” (see above).
Orals	Steroids designed for oral use.
Pyramiding	Process of slowly increasing the daily dose of anabolic steroids over time. When target dose is reached, the daily dose is then slowly reduced over time. Often done to avoid testing positive on urine or blood tests for steroids after competition.
Shotgunning	Taking steroids on an inconsistent basis.
Tapering	Slowly reducing one’s daily dose of steroids over a period of time.

SOURCE: Table based on Lukas (2014); Pope and Brower (2008); Pope and Kanayama (2015); Sagoe et al. (2015).

Many of these practices are quite common among individuals misusing steroids. For example, 61% of weightlifters using steroids were found to have engaged in the practice of “stacking” their steroid dose (Pope & Brower, 2004, 2005; Porcerelli & Sandler, 1998). Some of those who “pyramid” steroid doses are, at the midpoint of their cycle, taking massive doses of one or more compounds, although it should be noted that many who pyramid also intersperse periods of active steroid use with periods of total abstinence that might last weeks, months, or even as long as a year.⁶ Unfortunately, these periods of abstinence might be marked by the loss of much of their steroid-induced muscle mass, resulting in the individual returning to the use of anabolic steroids to recapture the lost muscle mass.

The Unknown Hazards of Steroid Misuse

The long-term effects of anabolic steroid misuse have only recently been studied in detail in the clinical literature, and much previous knowledge on their effects is based on use at therapeutic doses to treat disease (Pope & Brower, 2008; Pope & Kanayama, 2015). At therapeutic dosage levels, anabolic steroids can induce such side effects as sore throat, fever, vomiting (with or without blood being mixed with the material regurgitated), dark-colored urine, bone pain, unusual weight gain, headache, and a host of other effects (Congeni & Miller, 2002). However, those misusing anabolic steroids have been known to use dosage levels that are 40–100 to perhaps as much as 200 times the maximum recommended dosage level for these compounds (Congeni & Miller, 2002; Eisenberg & Galloway, 2005; Pope & Brower, 2008; Pope & Kanayama, 2015; Tomb, 2008). There is virtually no systematic information available about the effects of such dosage levels, and what little is known is based on anecdotal case reports of individuals misusing steroids.

It is known that the effects of anabolic steroids on muscle tissue will last for several weeks after the drug(s) are last administered, a characteristic that athletes often rely on to avoid having a positive urine toxicology test for performance-enhancing compounds after competition (Knight, 2003). It is also known that the adverse effects of anabolic steroid use depend on (a) the route by which the compound was administered, (b) the specific compound utilized, (c) the dosage level(s) utilized, (d) the frequency of steroid use,

(e) the general health of the individual, and (f) the age of the individual. Many individuals who misuse steroids view themselves, arguably with justification, as being more knowledgeable about the adverse effects of these compounds than physicians,⁷ often seeking to control these adverse effects without medical treatment (Hildebrandt et al., 2006; Pope & Brower, 2008; Pope & Kanayama, 2015). Most physicians are untrained in the recognition of steroid misuse, and in the past have tried to discourage anabolic steroid misuse by attempting to convince athletes that they were ineffective as muscle growth agents (Pope & Kanayama, 2015). Individuals misusing steroids thought they knew different, and thus the credibility of physicians as a source of information about anabolic steroid use and its consequences was destroyed (Pope & Brower, 2008; Pope & Kanayama, 2015; Stephens, 2008). Unfortunately, many who misuse steroids have turned to their suppliers or others misusing steroids through the use of social media as sources of information about steroids and their effects (Lukas, 2014; Pope & Brower, 2008; Pope & Kanayama, 2015). Ultimately, what is not known regarding the impact of anabolic steroid use and misuse for both short-term and long-term impact greatly outweighs what is known at this time (Pope & Kanayama, 2015).

Known Adverse Effects of Anabolic Steroids When Misused

On the Reproductive System

Males who use steroids, even at therapeutic dosage levels, might experience an enlargement of the breasts⁸ as the body converts the excess testosterone into estrogen (Botre & Pavan, 2008; Pope & Brower, 2009; Pope & Kanayama, 2015). This effect is more pronounced when the individual uses exceptionally high doses of steroids. Men who misuse steroids might also experience an increased frequency of erections, or a continual erection (known as **priapism**, a medical emergency). Men who misuse steroids might experience unnatural hair growth or loss, reduced sperm production, and an increased frequency of the urge to urinate, as well as degeneration of the testes, prostate gland enlargement, problems in urination, changes in libido, impotence, and sterility (Botre & Pavan, 2008; Eisenberg & Galloway, 2005; Pope & Brower, 2008; Pope & Kanayama, 2015; Schuckit, 2006a). Long-term steroid misuse might be a causal agent

⁶This makes the individual vulnerable to the “reverse anorexia nervosa” effect discussed earlier in this chapter, as the steroid-induced muscle mass is lost over time. The person becomes anxious about this process, and in many cases will restart the use of steroids to counter this process.

⁷Often for good reason, since most physicians are not trained to detect or treat steroid misuse.

⁸Technically, this condition is known as gynecomastia.

in the development of prostate cancer in some individuals (Pope & Brower, 2005). Ultimately, what is known thus far across studies of anabolic steroid use in men is that there can be serious and possibly long-term impacts on reproductive and related body systems (Christou et al., 2017).

Women who misuse anabolic steroids might become infertile, and may remain so for months or possibly years after their last use of steroids (Casavant et al., 2007). They might also experience an abnormal growth of the clitoris, irregular menstrual periods, unnatural hair growth or loss, a deepening of the voice, atrophy of the uterus, and a possible reduction in breast size (Botre & Pavan, 2008; Casavant et al., 1997; Pope & Brower, 2004, 2008; Pope & Kanayama, 2015; Schuckit, 2006a; Volkow, 2006b). The menstrual irregularities seen in females who use steroids may become permanent, as is true for many of the masculinizing effects induced in women who use steroids (Pope & Brower, 2005; Volkow, 2006b). In women, anabolic steroid use can have serious and possibly long-term impacts on reproductive and related body systems (Christou et al., 2017).

Effects of Anabolic Steroid Misuse on the Liver, Kidneys, and Digestive System

Individuals misusing steroids may experience altered liver function that may be detected on blood tests such as the serum glutamic-oxaloacetic transaminase (SGOT) and the serum glutamic-pyruvic transaminase (SGPT) tests (Karch, 2009; Sturmi & Diorio, 1998). Elevations on these tests are a sign of **hepatotoxicity**.⁹ There is evidence suggesting that, when used for periods of time at high dosage levels, steroids might contribute to the formation of both cancerous and benign liver tumors (Eisenberg & Galloway, 2005; Karch, 2009; Pope & Brower, 2005, 2008; Sturmi & Diorio, 1998). There is evidence that the form of liver tumor known as an adenoma may redevelop, or at least start to regrow, following steroid cessation (Martin, Abu Dayyeh, & Chung, 2008). This strongly suggests that steroid use “holidays”¹⁰ do not affect the growth of such liver tumors to any significant degree. There is also evidence pointing toward the risk of developing renal failure (Ostovar, Haerinejad, Farzaneh, & Keshavarz, 2017); in addition, steroid misuse may be important in consideration of the cause of kidney problems (Nanavati & Herlitz, 2017). Finally, anabolic steroid use might contribute to the retention of water in the body, increasing the work load on the heart (Botre & Pavan, 2008).

⁹See Glossary.

¹⁰Periods of time in which the individual does not abuse a given compound.

Anabolic Steroid Misuse and the Cardiovascular System

The heart is composed of muscle tissue, and it is strongly affected by the anabolic steroids (“Steroids and growth hormones make users ‘really ripped,’” 2003; Weiner et al., 2009). Habitual steroid use may result in 4–6 times higher incidence of sudden cardiac death (Belhani et al., 2009). Those who misuse steroids are more prone to heart disease than those who do not, possibly because of a dose-related cardiotoxic effect from anabolic steroids (Casavant et al., 2007; Eisenberg & Galloway, 2005; Montisci et al., 2012). This cardiotoxic effect is demonstrated by the necrosis of cardiac muscle tissue found in all who misuse steroids (Montisci et al., 2012). Other forms of steroid-related heart disease include hypertension, cardiomyopathy, and myocardial infarction. Ongoing steroid misuse induces a process known as “remodeling” of the heart, changes in the physical structure of the heart that alter its normal size and function. The left ventricle is especially vulnerable to the effects of the steroids, and is often found to be 25% thicker than in a healthy nonuser (Montisci et al., 2012).

Because of steroid-induced water retention, many individuals who misuse anabolic steroids develop edema in the hands and/or feet, which they often attempt to control by taking diuretic medication(s) (Eisenberg & Galloway, 2005; Schuckit, 2006a). Some who misuse steroids have been known to experience a drug-induced reduction of high-density¹¹ lipoprotein in the blood, while simultaneously increasing the low-density lipoprotein levels by as much as 36%. This contributes to accelerated atherosclerosis of the heart and surrounding blood vessels (Kanayama et al., 2006; Pope & Brower, 2005).

Steroid Misuse and the Central Nervous System

It is now accepted that anabolic steroid misuse can induce behavioral changes in the individual, although most individuals are reluctant to attribute their neuropsychiatric problems to their steroid misuse (Pope & Brower, 2008; Pope & Kanayama, 2015; Pope, Kouri, & Hudson, 2000). There are no premorbid signs that would warn the individual that s/he is at risk for steroid-induced neuropsychiatric problems (Pope et al., 2000). However, some individuals who regularly use anabolic steroids experience a sense of **dysphoria**,¹² or even clinically significant depressive reactions, especially during the withdrawal phase following prolonged periods

¹¹The so-called “good” cholesterol.

¹²See Glossary.

of steroid misuse (Kilmer, Palmer, & Cronic, 2005; Pope & Brower, 2004, 2005, 2008; Pope & Kanayama, 2015; Schuckit, 2006a). Steroid withdrawal depression appears to respond well to psychotherapy and the use of selective serotonin reuptake inhibitors (SSRIs) (Pope & Brower, 2008), but in severe cases further steps to balance endocrine functioning will need to be taken (Pope & Kanayama, 2015). It is important to keep in mind that suicide is a frequent complication of depression, and approximately 4% of those who have misused steroids have made at least one serious suicide attempt (Pope & Brower, 2008).

Individuals who misuse anabolic steroids are thought to be at risk for a drug-induced psychosis and the development of a condition known as “[ste]roid rage” (Botre & Pavan, 2008; Eisenberg & Galloway, 2005; Pope & Brower, 2004, 2005). There is an association between steroid use and aggression, but most studies exploring this problem have been correlational,¹³ and some research studies have yielded contradictory findings (Shaffer, 2015). Although the exact relationship between steroid use and violence has yet to be determined, preliminary evidence does suggest a possible relationship, prompting Pope and Brower (2004) to suggest that large, muscular perpetrators of interpersonal violence be screened for steroid use upon arrest. These episodes of steroid-associated anger appear to be the outcome of drug-related changes in the GABA_A, dopamine, and serotonin receptor sites in the mesolimbic region of the brain.¹⁴

Although these reactions are attributed to steroid misuse, there is also the possibility that individuals who become violent while taking steroids might have a history of criminal thinking and antisocial behavior that *predates* their steroid use (Klotz, Garle, Granath, & Thiblin, 2006). Such individuals would be “at risk” for impulsive behaviors such as reacting with violence, which then would be attributed by researchers to their steroid use rather than their predisposing personality, according to Klotz and colleagues (2006). While this hypothesis is interesting, it has yet to garner significant research investigation, and thus is but one possibility for the apparent connection between steroid misuse and violent behavior.

Other Steroid-Related Disorders

Patients with medical conditions such as certain forms of breast cancer, diabetes mellitus, blood vessel disease, kidney, liver or heart disease, and men with prostate disease should not use anabolic steroids except if directed to do so by a physician who is aware that the patient has these problems

(Eisenberg & Galloway, 2005). There is evidence that anabolic steroid use contributes to, if not causes, cancer, and their use is not recommended for patients with either active tumors or a history of either benign or cancerous tumors, except if directed to do so by a physician who supervises the patient during the period of steroid use.

Other side effects caused by steroid misuse include severe acne, especially across the back (“steroid acne”), which some patients attempt to control by taking illicit antibiotics, and oily skin (Botre & Pavan, 2008). The individual might develop a foul odor on the breath (Casavant et al., 2007). Further, animal research suggests that anabolic steroid abuse may contribute to tendon degeneration, possibly to the point where the tendon might rupture under stress (Casavant et al., 2007; Eisenberg & Galloway, 2005). Adolescents who misuse anabolic steroids are vulnerable to premature cessation of bone growth as the growth plate at the end of the bone prematurely fuses (Casavant et al., 2007). It has also been suggested that anabolic steroids might be a gateway to other drug use as the abuser attempts to cope with muscle-related pain, acne, and other steroid-related problems (Kanayama, Cohane, Weiss, & Pope, 2003). Finally, if the individual should share needles with others who are injecting steroids, an all too common practice, s/he is vulnerable to the acquisition of various blood-borne infections (Eisenberg & Galloway, 2005; Pope & Kanayama, 2015).

Drug Interactions Between Anabolic Steroids and Pharmaceuticals

The anabolic steroids interact with a wide range of medications used to treat disease states and with many of the drugs that are misused. There is evidence of an interactional effect between acetaminophen¹⁵ and anabolic steroids. Further, alcohol-dependent patients on Antabuse (disulfiram) should not take anabolic steroids, nor should patients who are taking the medication naltrexone, or the anticonvulsant medications such as phenytoin, valproic acid, or any of the phenothiazine class of antipsychotic medications. This is only a partial list of the possible steroid–medication interactions, and a pharmacist should be consulted about such possible interactions.

Are Anabolic Steroids Addictive?

A quarter of a century ago, most physicians would have offered an unqualified answer of “no.” Although the question is still being debated, evidence would suggest that

¹³As statistics instructors repeatedly remind their students, *correlation does not imply causality*.

¹⁴Brain regions involved in the fight-or-flight response.

¹⁵Discussed in the next chapter.

this answer is wrong (Pope & Brower, 2008; Pope & Kanayama, 2015). Clinical evidence would suggest that anabolic steroid dependence rests on three pillars: (1) the individual's *psychological* reliance on steroids ("I need steroids to bulk up"), (2) the individual's perceived past benefit from past steroid misuse, and (3) ultimately the development of physical withdrawal symptoms. The psychological dependence on anabolic steroids rests upon the belief that the individual needs steroids to avoid the loss of muscle mass, or to maintain one's attractiveness to the opposite sex.

The second factor, perceived benefit, rests on a foundation of external feedback ("you look great" or "your endurance is improving"), functions to encourage continued steroid abuse, as well as self-perception. Persons who are using high doses of anabolic steroids report a mild sense of euphoria from anabolic steroids, which serves as an additional incentive to continue misusing these compounds. The euphoric effects of anabolic steroids are assumed to be approximately the same as caffeine, nicotine, or possibly the benzodiazepines (Wood, 2004). Steroid-induced euphoria may reflect the impact of these compounds on the mesolimbic system, especially the dopamine neurotransmission system (Pope & Brower, 2005; Wood, 2004).

Many individuals who use steroids chronically experience a protracted withdrawal syndrome when they discontinue steroid use, and might experience symptoms such as loss of muscle mass, insomnia, fatigue, dysphoria, restlessness, anorexia, headaches, lowered libido (Kilmer et al., 2005; Lukas, 2014; Pope & Brower, 2005; Pope & Kanayama, 2015), and, as noted earlier, the development of a depressive reaction that might reach suicidal proportions. Gradual detoxification from steroids and intensive psychiatric support limit the impact of these symptoms on the individual's life. Not surprisingly, the diagnostic signs of steroid use disorder are virtually the same as those for other drugs that are misused, supporting the hypothesis that steroids are indeed addictive.

Anabolic Steroid Use Disorder and the Diagnostic and Statistical Manual of Mental Disorders (5th Edition)

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) does not directly address the problem of anabolic steroid misuse. By default, it falls within the domain of the "other substance use disorder" category, which it shares with the unknown substance use disorders. The

DSM-5 identified five subforms of the other substance use disorders:

- *Other (or unknown) substance use disorder*
- *Other (or unknown) substance intoxication*
- *Other (or unknown) substance withdrawal*
- *Other (or unknown) substance-induced disorders*
- *Unspecified other (or unknown) substance-related disorders*

The first requirement for a diagnosis of an *other (or unknown) substance use disorder* is the "problematic pattern of use of an intoxicating substance" (American Psychiatric Association, 2013, p. 577) that does not fall within the other categories of substance use disorders. The anabolic steroids most certainly meet the latter part of this requirement; however, as discussed earlier in this chapter, many individuals who misuse steroids use these compounds not for their intoxicating effects (which are limited), but for their ability to aid the development of muscle tissue. Thus, steroids only partially meet the first part of the requirement in most situations, since few individuals who use steroids do so to seek a sense of intoxication from these compounds. The DSM-5 identifies 11 criteria, two of which are the development of tolerance and a withdrawal syndrome, with two of the 11 criteria within a 12-month period being sufficient to diagnose the individual with an *other (or unknown) substance use disorder*. The reader is referred to the DSM-5 for the full list of diagnostic criteria suggested by the American Psychiatric Association (2013) as signs of an *other (or unknown) substance use disorder*.

The category *other (or unknown) substance intoxication* is of dubious applicability to those who use steroids, in that there is no characteristic pattern that would suggest steroid "intoxication." Although there is a steroid withdrawal process, it is not clear whether this meets the criteria for this diagnosis in the DSM-5. Most certainly, anabolic steroid misuse contributes to the development of various medical and psychiatric conditions, and thus careful consideration of *other (or unknown) substance-induced disorder* should be made when working with individuals who have misused steroids.

Are Misused Steroids Effective?

It might strike the reader as somewhat ironic that this discussion follows the sections of this chapter discussing the phenomenon, scope, and identified dangers of anabolic steroid misuse. However, this irony is tempered by the fact that the possibility exists that the anabolic steroids might not live up to their reputation, given the need for much more

testing in human (Lukas, 2014). Some individuals use steroid intended for use in humans at levels hundreds or even more than a thousand times the maximum therapeutic dose, and often inject steroids at these supra-normal dosage levels. Further, those misusing steroids often use steroids meant for animal use, injecting¹⁶ these compounds into their bodies in massive quantities.

There are three main reasons why anabolic steroid use may be effective: (1) the **placebo effect**,¹⁷ (2) the fact that those persons most likely to misuse anabolic steroids are also more likely to eat healthy diets to assist them in achieving peak performance in their sport(s) of choice or to look their very best, and (3) that it would be grossly unethical to administer such huge doses of steroids in the manner in which they are misused to a control group of non-athletes to provide an objective measure of the effectiveness of steroids at such high doses. So the answer is, we do not know if they are effective or not.

¹⁶Sometimes sharing the needle, exposing those who share the needle to all the blood-borne diseases found within the first user's blood.

¹⁷See Glossary.

Chapter Summary

The anabolic steroids emerged as drugs of misuse in the latter part of the 20th century, with several subgroups of individuals who misuse these substances emerging over the years. But the dynamics of steroid misuse differ from those of other, more traditional drugs of misuse. The primary reasons why anabolic steroids are misused is not for their euphoric effects (although anecdotal reports indicate that anabolic steroids do induce euphoria), but for their effects on muscle development. Some adolescents and young adults believe that the steroids will help them achieve a better physical appearance, while athletes believe that since the competition is using steroids, they must do so in order to “level the playing field.” Both groups continue to engage in anabolic steroid misuse in spite of the knowledge that these compounds alter the normal function of the central nervous system, and can cause premature termination of bone growth and cardiovascular damage that will be with them for the rest of their lives. The identification and treatment of steroid misuse is primarily a medical issue, although substance rehabilitation professionals play an important adjunctive role in this process and thus should have a working knowledge of anabolic steroid misuse.



CHAPTER 15

Tobacco Products and Tobacco Use

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 15.1** Understand the history of tobacco use in the United States
- 15.2** Understand the scope of the problem of tobacco use
- 15.3** Comprehend the pharmacology, methods of use, and subjective effects of tobacco
- 15.4** Describe the complications of long-term use of tobacco
- 15.5** Describe the concerns regarding secondhand smoke
- 15.6** Explain the benefits of smoking cessation
- 15.7** Understand the *DSM* criteria for tobacco related disorders

Introduction

Biologists suggest that nicotine, which would become known as the active agent in tobacco, emerged as a natural form of insect repellent. The first peoples of North and South America found that they enjoyed the effects of tobacco, and by 8,000 years ago its use was widespread throughout the two continents. By 7,000 years ago, the people living in Peru and Ecuador were actively cultivating tobacco (Burns, 2007). It was used in religious and social ceremonies, and when the smoke of the tobacco plant was delivered rectally, it was thought to be a useful medicine (Burns, 2007). The first written reference to tobacco was found in a Mayan carving, which is thought to have been made more than 2,600 years ago (Schuckit, 2006a).

Then the first European explorers arrived, and, for all concerned, the world changed. The practice of tobacco smoking was carried back across the Atlantic to Europe by the early European explorers, who had adopted the habit of smoking while in the New World. The practice of smoking initially met with some skepticism, if not outright hostility. In Germany, public smoking was deemed a crime that could be punished by death, while in Russia, castration was the sentence for same offense (Hymowitz, 2005).¹ In Asia, the use or distribution of tobacco was a crime punishable by death, and smokers were executed as infidels in Turkey. In spite of

¹Readers may decide for themselves which punishment was the greater incentive for smoking cessation.

these sanctions, the practice of smoking tobacco continued to spread across Europe and into Asia (Schuckit, 2006a).

Fifteenth-century European physicians believed tobacco had medicinal properties, in part because they had so few medications that worked. Further, the social use of tobacco products gained acceptance as a sign of sophistication and social status in Europe and the Americas. However, in the last half of the 20th century, physicians began to identify long-term consequences of tobacco smoking, and a campaign against its use began, in spite of efforts on the part of the tobacco industry to disprove any claims of harm from its products. In the 21st century, tobacco use remains widespread, controversial, and the subject of much debate. In this chapter, the practice of using tobacco, and the complications associated with its use, will be reviewed.

A Very Short History of Tobacco Use in the United States

Anthropologists now believe that tobacco was actively being cultivated in South America as early as 8,000 years ago (Burns, 2007; Walton, 2002). However, this was not the same form of tobacco that we know today. The original strain(s) of tobacco were more potent, and possibly might have contained hallucinatory compounds not found in today's tobacco (Schuckit, 2006a; Walton, 2002). European smokers preferred the milder *Nicotiana tabacum* over the more potent *Nicotiana rustica* commonly used by the natives of the New World, and this is the form of tobacco that was cultivated by the first settlers from Europe (Burns, 2007). Arguably, the establishment of the first European colonies in the New World was fueled, in part, by the demand for tobacco in Europe. So highly valued was tobacco that it actually functioned as a form of currency in certain colonies (Burns, 2007).

At the time, the preferred method of tobacco use was by smoking, although there were those who insisted on chewing the tobacco leaf, either spitting the expectorant out, or, if they were from the upper classes, swallowing it. Tobacco played an interesting role during the Civil War: Soldiers from both sides would arrange for an informal truce from time to time to barter tobacco for coffee and sugar. By the mid-19th century, several forces combined to change the shape of tobacco use. First, new varieties of the tobacco plant were developed that provided greater yields. New methods of curing tobacco leaves were developed, allowing for a more rapid transit from harvest to arrival at the manufacturer's facility. Cigarettes, a smaller, less expensive, and neater way to smoke than was

possible with cigars, were introduced. Machinery capable of manufacturing large numbers of cigarettes was introduced: Just one machine, invented by James A. Bonsack, could produce 120,000 cigarettes a day, far in excess of what could be made by hand.

The introduction of machinery to the manufacturing process allowed for the sale of cigarettes to members of lower social classes, as the cigarette was now affordable to virtually everybody. Simultaneously, it was discovered that the practice of chewing tobacco and spitting the expectorant into the ever-present cuspidor contributed to the spread of tuberculosis and other diseases. In a piece of historical irony, public health officials began to endorse cigarette smoking as a safer, sanitary, relatively inexpensive substitute for tobacco chewing. Unlike those who smoked pipes or cigars, those who smoked cigarettes discovered that the smoke from their cigarettes was so mild that it could be inhaled. The practice of cigarette smoking quickly became the preferred method of tobacco use in the United States, although there were (and remain) those who preferred to chew tobacco.

Scope of the Problem of Tobacco Use

Globally, cigarette smoking is a \$400 billion/year industry, with an estimated 800 million men and approximately 200 million women on this planet smoking each day (Levititz, Bradley, & Golden, 2004; Rose et al., 2003; World Health Organization, 2006). It has been estimated that 15 billion cigarettes are sold each day around the world, with China continuing as the largest consumer of tobacco ("China's healthcare woes," 2008; Tobacco, 2009; World Health Organization, 2017b). So popular is the practice of cigarette smoking around the world that the global per capita consumption of cigarettes is estimated at 1,000 for every man, woman, and child on earth (Sundaram, Shulman, & Fein, 2004).²

In the United States, 387.6 billion cigarettes are consumed each year (Kaufman, 2006). In contrast to the 1950s, when approximately half of the adult population smoked cigarettes, just under 18% continue to smoke cigarettes (U.S. Preventive Services Task Force, 2015). Comparing this with the SAMHSA (2017) statistic indicates that for all tobacco products, the percentage is close to 24% for use in the past month by those 12 and over. While cigarette use decreased by 32.8% in the period from 2000 to 2011, the use of pipe

²This figure is for every person on earth, not just those who smoke cigarettes.

tobacco increased by 5.8% and cigars increased by 3.33% (Tynan, McAfee, Promoff, & Pechacek, 2012), suggesting that at least some individuals who formerly smoked cigarettes have switched to these alternative methods of tobacco use. The percentage of those who formerly smoked cigarettes who have switched to electronic cigarettes is not known at this time. It is not uncommon for subpopulations of individuals to have different concordance rates than the general population. For example, it has been estimated that between 71 and 100% of persons with a substance use disorder smoke cigarettes (el-Guebaly, Cathcart, Currie, Brown, & Gloster, 2002) while at least 90% of individuals diagnosed with schizophrenia also smoke cigarettes (Pankiewicz, 2008). Overall, it is estimated that those who have SUDs or mental health diagnoses use 44% of the cigarettes in the United States (Kalman, Hayes, & Ziedonis, 2015).

The scope of cigarette smoking thus demonstrates wide variance around the globe, a variance explained in part by how accepting the culture is of cigarette smoking. In the United States, there is a tacit if not vocal disapproval of cigarette smoking except among members of certain subgroups such as those who actively misuse drugs. In contrast to this, the culture in China is more accepting of cigarette smoking, especially by men. As will be discussed in Chapter 20, a large percentage of children have taken at least one puff of a cigarette and have formed opinions that are more or less accepting of cigarette smoking, suggesting that the roots of the tobacco use disorders often lie in childhood, but only find full expression a decade or more later during the individual's adult years.

The Pharmacology of Cigarette Smoking

The primary method of tobacco use is cigarette smoking,³ although chewing tobacco and cigar smoking have both gained popularity in some circles (Schuckit, 2006a). The invention of electronic cigarettes and similar products will certainly impact future trends. Chemically, cigar smoke is very similar to tobacco smoke, although it does contain a higher concentration of ammonia, and the nicotine is absorbed through the mouth and the upper respiratory tract as opposed to the nicotine from cigarettes, which is absorbed in the lower respiratory tract (Burns, 2008; Lehne, 2013). This is due in part to the fact that cigar smoke is too alkaline for the individual to comfortably inhale very deeply.

³For this reason, the words *cigarette smoking*, *smoking*, and *tobacco* use will be used interchangeably in this chapter, unless stipulated otherwise.

The main psychoactive compound in tobacco is nicotine. However, this is but one of thousands of chemicals found in tobacco smoke, the exact composition of which is influenced by a number of variables, including (Dani, Kosten, & Benowitz, 2009) (1) the exact composition of the tobacco being smoked, (2) how densely the tobacco is packed, (3) the length of the column of tobacco (for cigars and cigarettes), (4) the characteristics of the filter (if any), and (5) the temperature at which the tobacco is smoked. Many studies of the composition of cigarette smoke were conducted in the 1960s, and this data is still often referenced in professional journals. The observed changes in the composition of cigarettes over decades raise questions about the relevance of research studies conducted in the 1960s to the contents of tobacco smoke in the modern cigarette. Up to 40% of an average cigarette is composed of “leftover stems, scraps and dust” (Hilts, 1996, p. 44), some of which may be swept off the floor before being added to the tobacco. Whereas in 1955 it took 2.6 pounds of tobacco to produce a thousand cigarettes, the use of these fillers has made it possible to produce a thousand cigarettes with only 1.7 pounds of tobacco (Hilts, 1996). These manufacturing practices allow for a 44% profit margin per pack of cigarettes sold (Fonda, 2001). As will be discussed later in this chapter, there is strong evidence that nicotine is being added to the raw cigarette by the manufacturer, making it more addictive than the cigarette of 1950.

Researchers have isolated some 4,700 chemicals from tobacco smoke, of which 2,550 come from the unprocessed tobacco itself (Fiore, 2006; Schmitz & Delaune, 2005; Stitzer, 2003). Waste from production as well as use of tobacco products contains more than 7,000 chemicals (World Health Organization, 2017b). A partial list of the compounds known to be in tobacco smoke includes:

Acetaldehyde, acetone, aceturitrile, acrolein, acrylonitrile, ammonia, arsenic, benzene, butylamine, carbon monoxide, carbon dioxide, cresols, crotonitrile, DDT, dimethylamine, endrin, ethylamine, formaldehyde, furfural hydroquinone, hydrogen cyanide, hydrogen sulfide, lead, methacrolein, methyl alcohol, methylamine, nickel compounds, nicotine, nitric oxide, nitrogen dioxide, phenol, polonium-210 (radioactive), pyridine, “tar” (burned plant resins)

*Shipley & Rose, 2003, p. 83,
bold in original deleted*

Individuals who smoke cigarettes are also exposed to low levels of a known poison, arsenic, as a result of their smoking. Cigarette smoke contains at least 1,000 times the levels of radioactive gasses such as radium and polonium that were

contained in the fallout from the nuclear reactor in Chernobyl, Ukraine, when it exploded in the 1980s (Papastefanou, 2007). These compounds are found naturally in the soil, are concentrated in the tobacco plant as it grows, remain in the leaves when they are harvested, and when the individual inhales, they are carried into the lungs. The tobacco industry was aware of this fact more than 50 years ago, but suppressed this research to avoid alarming those who smoke about radioactive compounds in cigarette smoke (Muggli, Ebbert, Robertson, & Hurt, 2008). Because of this fact, it was recommended that the standard federally mandated warning labels on the side of cigarette packages be modified to carry a radiation exposure label (Muggli et al., 2008). However, this proposal was not enacted.

During the time before harvest, the tobacco plant is exposed to various herbicides, fungicides, and rodenticides that were sprayed on the tobacco. Then there are the compounds found in the burning cigarette wrapper or that are formed when the paper is burned, as well as the various machine lubricants that drip into the tobacco or wrapping paper as they move along in the manufacturing process (Glantz, Slade, Bero, Hanauer, & Barnes, 1996). Finally, there are the various perfumes that are added to the tobacco to give it a characteristic aroma (Hilts, 1996). Depending on the specific brand, the individual will inhale molecules of some or all of these products when s/he smokes; however, there has been virtually no research into the pharmacokinetic or toxicological effects of these compounds in the human body.

In response to challenges that cigarettes were dangerous to the individuals smoking them, the tobacco industry introduced “light” or “filtered” forms of established brand names to give the illusion that they were safer. In reality, these changes did little to reduce the individual’s level of exposure to the toxins found in cigarette smoke (Hilts, 1994; Pennock, 2007). This is seen, for example, in the research finding that those who smoke “light” cigarettes have the same coronary artery problems as those who smoke regular brands, and that these cigarettes were just as addictive as regular cigarettes (Gullu et al., 2007; Hymowitz, 2005; “Light cigarettes just as addictive as ‘full flavored,’” 2006).

Electronic Nicotine Delivery Systems (ENDS)

In 2003, the “electronic” or e-cigarette was invented. They were originally crafted to resemble regular tobacco cigarettes, but now take a variety of forms, including what is often referred to as a vaporizer. E-cigarettes and vaporizers are battery-operated and designed to deliver a refined, aerosolized nicotine mist to the user. They have rapidly become popular, and in 2014, almost 15% of adults in the United States

had tried ENDS, and close to 5% regularly used such devices (Weaver et al., 2016). Because they have only recently been introduced, the long-term effects of ENDS use have not been explored (de Lange, 2014). ENDS avoid exposing the user to many of the toxic chemicals found in regular cigarettes, and it has been estimated that they pose only 5% of the risk to the individual smoking them as regular cigarettes (McNeill, Brose, Calder, & Hitchman, 2016), apparently making it a safer alternative to regular cigarettes. However, the team of Jensen, Lou, Pankow, Strongin, and Peyton (2015) found that e-cigarette use exposes the user to formaldehyde, a chemical preservative often used in embalming bodies. There is also evidence that at least some varieties of e-cigarettes contain alcohol, which is inhaled when the individual smokes these e-cigarettes, although the effects of this alcohol exposure on the user are not known at this time (Valentine et al., 2016). There is little evidence that e-cigarettes might serve as a gateway to other forms of tobacco use in later life (McNeill et al., 2016), although this conclusion has been challenged (de Lange, 2014). The level of nicotine varies from brand to brand, and in the United States the Centers for Disease Control has moved to regulate such products through its Center for Tobacco Products.

Nicotine

This compound was first isolated by chemists in 1828, and in 1889, nicotine’s effects on nervous system tissue were first identified. A century later, scientists are still attempting to understand all of nicotine’s effects on the central nervous system (Stitzer, 2003). Such research is important since nicotine is the primary reinforcing agent in tobacco. What might loosely be called “big tobacco”⁴ knew for decades that nicotine was the major psychoactive compound in cigarettes, and that cigarettes were little more than single-dose administration systems for nicotine (Glantz et al., 1996; Hilts, 1994, 1996). This is supported by the observation that cigarette manufacturers increased the nicotine content of most major brands of cigarettes by 10% between 1998 and 2004 (Brown, 2006). Much research is being conducted to push forward support for reducing the nicotine content of cigarettes, with hopes for a positive public health impact (Benowitz, Donny, & Hatsukami, 2017; Donny et al., 2017).

Since it avoids the risk of the first-pass metabolism process, cigarette smoking is viewed as the ideal method by which to introduce nicotine into the body. Each puff of a cigarette introduces a small dose of nicotine, which then reaches the brain in a matter of seconds (Gwinnett & Adamec, 2006;

⁴Major cigarette producers.

Kalman et al., 2015; Stahl, 2008). The individual who smokes one pack a day self-administers approximately 85,000 puffs on cigarettes each year, consuming 7,000 cigarettes in doing so (Shadel & Scharf, 2012),⁵ with each “puff” initiating a small reward cascade for the individual. In the brain, nicotine breaks down the levels of an enzyme known as monoamine oxidase β . This enzyme normally helps to break down dopamine after its release into the synapse. The current theory is that by reducing brain monoamine oxidase β levels, dopamine will have a stronger effect at its receptor sites, indirectly activating the brain's reward system. Further, nicotine stimulates the release of small amounts of nitric oxide in the brain, which again has the effect of slowing down the process of dopamine reuptake. This combined action results in the dopamine that is released having a stronger and more prolonged effect (Fogarty, 2003). Nicotine also binds at the acetylcholine receptors in the brain. This indirectly induces the release of vasopressin, GABA, glutamate, beta endorphin (β endorphin), and **epinephrine**⁶ when the individual inhales the smoke (Bacher, Rabin, Woznica, Sacco, & George, 2010; Fogarty, 2003; Gwinnell & Adamec, 2006; Hymowitz, 2005; Schmitz & Delaune, 2005).

Nicotine-induced epinephrine release contributes to the individual's sensation of alertness and reduced fatigue, while many of the other compounds released when the individual smokes are involved in the sensation of relaxation or pleasure. This might be why many individuals who smoke believe that smoking helps them calm down during times of stress. The team of Gehricke and colleagues (2009) examined the mechanics of nicotine-induced relaxation through **PET scans**,⁷ and found that individuals who had nicotine in their systems demonstrated a change in brain metabolism in such a way that it interfered with the cortical and subcortical regions of the brain responsible for the integration and expression of emotions with perceptions. This would appear to contribute to the individual's sense of relaxation under stress. However, it should be noted that for some unknown reason the clinical effects of nicotine are different for those persons who struggle with a psychiatric disorder as compared with normal individuals (Bacher et al., 2010).

It has been found that nicotine induces a total saturation of one of the 12 known subtypes of the acetylcholine receptor in the brain (Brody et al., 2006; Stahl, 2008). Long-term binding at this acetylcholine receptor site subtype⁸ induces

desensitization, a process that by coincidence takes about as long as it takes to smoke just one cigarette (Stahl, 2008). Resensitization begins almost immediately, resulting in a state in which receptor sites not occupied by nicotine molecules cause or exacerbate withdrawal symptoms experienced between cigarettes, restarting the cycle as the individual lights another cigarette (Brody et al., 2006; Stahl, 2008). This cycle takes about 45 minutes, the result being that a person who smokes a pack a day can keep this acetylcholine receptor subtype desensitized throughout the day (Stahl, 2008). This helps the individual feel relaxed as a result of smoking, and contributes to the experience of craving when the person quits smoking.

Peak concentrations of nicotine are achieved in the first few minutes after smoking a cigarette, and then drop as the nicotine is redistributed to blood-rich body tissues. The biological half-life of nicotine is approximately 2 hours (Dani et al., 2009; Hughes, 2005; Kalman et al., 2015). Since only 50% of the nicotine from each cigarette is biotransformed in the first half-life period, a reservoir of nicotine that has not been biotransformed or excreted builds up in the body. This reservoir is constantly renewed as the individual continues to smoke. A limited degree of tolerance to nicotine does develop during the day, but is just as rapidly lost in the night hours when the average person who smokes abstains (Hughes, 2005). This is why many individuals who smoke report that the first cigarette in the morning has such a strong effect on them.

The majority of the nicotine absorbed into the body is metabolized in the liver before elimination, and only 5–10% is excreted unchanged (Dani et al., 2009; Hymowitz, 2005). The majority of nicotine is biotransformed into *cotinine*, a metabolite that in recent years has been found to have a psychoactive action of its own, biotransformed into trans-3'-hydroxycotinine (3HC) (Kalman et al., 2015; Schmitz & Delaune, 2005). Although it was once thought that individuals who smoke cigarettes were able to biotransform nicotine more rapidly than those who do not smoke, research has failed to support this belief, although it is acknowledged that there is genetic, racial, and gender variation in the speed with which individuals are able to biotransform nicotine into its metabolites prior to elimination (Kalman et al., 2015).

Acetaldehyde

Tobacco smoke also contains a very small amount of acetaldehyde. This is the first metabolite of ethyl alcohol that is produced when it goes through the biotransformation process. Research has demonstrated that acetaldehyde that is absorbed will bond with the saliva. This in turn allows the toxin to remain in contact with oral tissues longer, increasing the individual's risk of oral cancers (Melton, 2007).

⁵Through sheer repetition this becomes a habitual behavior through the process of “over-learning.”

⁶Also known as adrenaline.

⁷See Glossary.

⁸Known as the $\alpha 4\beta 2$ nicotinic acetylcholine receptor subtype, in case you wondered.

Drug Interactions Between Nicotine and Prescribed Medications

Nicotine is biotransformed through the cytochrome P-450 metabolic pathway in the liver, altering the pharmacokinetics of numerous other compounds that are biotransformed by this same metabolic pathway. For example, it is known that individuals who smoke cigarettes will require more morphine for pain control than individuals who do not smoke. Individuals who smoke cigarettes will also have lower blood plasma concentrations of such compounds as propranolol, haloperidol at a given dosage level than will those who do not smoke (Dani et al., 2009; Hughes, 2005). Individuals who smoke tobacco may experience less sedation than those who do not smoke tobacco when administered a given dose of a benzodiazepine, but appear to be able to biotransform marijuana more rapidly than those who do not smoke (Nelson, 2000).

Tobacco also interacts with many anticoagulants such as Warfarin® (Ellingrod, 2013), making it difficult to achieve adequate coagulation control. Women who use oral contraceptives and who smoke are at significantly higher risk for stroke, myocardial infarction, and thromboembolism compared with women the same age who do not smoke (Dani et al., 2009). When individuals who use theophylline quit smoking, they experience a significant rise in theophylline levels in the first week of abstinence. Further, blood levels of caffeine might increase by as much as 250% following smoking cessation, causing caffeine-induced anxiety symptoms for the individual. Anxiety is also an early symptom of nicotine withdrawal, which the smoker quickly learns to self-medicate by smoking another cigarette and stopping the withdrawal symptoms before they develop.

Nicotine appears to decrease the blood levels of clozapine and haloperidol by as much as 30–50% as a result of its ability to induce the biotransformation of these compounds, thus reducing their effectiveness (Ellingrod, 2013; Kavanagh, McGrath, Saunders, Dore, & Clark, 2002). At the same time, it blocks the biotransformation of the antidepressant medications desipramine, doxepin, and nortriptyline, raising blood levels of these compounds. These nicotine–drug interactions can complicate the patient’s treatment and interfere with the patient’s response to prescribed medications.

It has been discovered that 66% of individuals dependent on alcohol also smoke, possibly because nicotine is more reinforcing for these individuals than it is for the individual who does not drink (Kalman et al., 2015).⁹ This may reflect the fact that nicotine addiction is mediated by many of the

same genes that are thought to trigger alcohol dependence (Le et al., 2006). Further, the stimulant effects of nicotine appear to counteract some of the sedation induced by the individual’s alcohol use, allowing the individual to drink more, or drink longer. Because of the vasoconstrictive effect of cigarette smoke, it takes longer for an insulin-dependent diabetic to absorb transdermal injections of insulin, making blood glucose control more difficult (Dani et al., 2009). While this list of possible interactions between cigarette smoke and medications does not discuss every possible interaction effect, it does demonstrate that nicotine is a very potent compound, with the ability to influence the pharmacokinetics of many pharmaceuticals currently in use.

The Effects of Nicotine on the Body

Nicotine is quite toxic, and the estimated lethal dose for an adult is 40–60 mg (Hymowitz, 2005; Lehne, 2013). Orally administered nicotine in adults is subjected to the first-pass metabolism effect, limiting its effect on the individual. Symptoms of nicotine toxicity include nausea, vomiting, diarrhea, abdominal pain, headache, sweating, and pallor (Hymowitz, 2005).¹⁰ Oral overdoses can also result in symptoms such as dizziness, weakness, confusion, coma, and possible death from respiratory paralysis. These symptoms are very similar to those reported by first-time smokers, suggesting that they also demonstrate nicotine toxicity as a result of their first cigarette use. The bodies of children are able to absorb nicotine from the gastrointestinal tract more effectively than adults, and they are more likely to orally ingest tobacco products rather than smoke them, making a tobacco overdose especially dangerous in children.

The degree of discomfort experienced by the individual who begins to smoke appears to be mediated, in part, by his or her genetic heritage (Whitten, 2011). As the individual persists in his or her efforts to continue to smoke, the stimulation of the neurotransmitter systems involved in the reward cascade will help the individual new to smoking learn to associate the practice of smoking with pleasure and relaxation (Kalman et al., 2015). In the body, nicotine stimulates the release of acetylcholine, which controls many body functions. This may account, at least in part, for nicotine’s effects on the cardiovascular system, such as the increase in heart rate and blood pressure, and the increased strength of heart contractions observed after a person smokes a cigarette. Nicotine also induces a reduced rate and strength of muscle contractions in the stomach, and causes the blood vessels in the peripheral

⁹Some individuals have reported that they smoke *only* when they are drinking, and that they can abstain from cigarettes between periods of alcohol use.

¹⁰Any real or suspected overdose should always be assessed by a physician immediately.

regions of the body to constrict (Schuckit, 2006a). The process of smoking deposits many potentially harmful chemicals in the lungs, possibly contributing to the decreased action of the *cilia*¹¹ in the lungs. These nicotine-induced effects seem to account for at least some of the pulmonary problems seen in those who smoke chronically.

Nicotine Addiction

Although this information was not discussed in public for many years, researchers for various tobacco companies have known since the early 1960s that tobacco products were highly addictive. This discovery was promptly suppressed by the tobacco industry (Hurt & Robertson, 1998; Slade, Bero, Hanauer, Barnes, & Glantz, 1995). Indeed, one industry memo from 1963 released by court order was cited by Slate and colleagues (1995) as an illustration of how the tobacco industry knew that it was “in the business of selling nicotine, an addictive drug” (p. 228). However, it was not until 1997 that major a single tobacco company in the United States admitted in court that tobacco was addictive (Solomon, Rogers, Katel, & Lach, 1996).

Current research suggests that besides nicotine, a range of other compounds appear to contribute to the development of an addiction to tobacco products, although at this point nicotine is considered the most potential addiction-inducing compound found in tobacco. Some of these other compounds include anbasine, nornicotine, anatabine, cotinine, myosmine, and acetaldehyde (Hurley, 2014). However, scientists are still exploring the contribution of these other compounds to tobacco addiction, and we will limit our discussion to the most studied of the compounds found in tobacco: nicotine.

Like the other drugs that are misused, nicotine alters the firing pattern of neurons in the nucleus accumbens region of the brain (Kalman et al., 2015). Surprisingly, the compound that is closest to producing the same pattern of altered neural function induced by nicotine use is the opioid family of compounds (Britt & McGehee, 2008). This makes clinical sense, since smokers report a sense of pleasure when they smoke, suggesting that nicotine stimulates the release of endogenous opioids in the brain. The addictive potential of nicotine would seem to be higher than that of cocaine, as illustrated by the fact that while 3–20% of those who try cocaine become addicted to it, at least 33–50% of those who experiment with cigarette smoking become addicted¹² to the

practice (Oncken & George, 2005). Further, like the other drugs, the greater the individual's exposure to nicotine, the greater the chance that she or he will become addicted to this compound.

Scientists have documented physical changes in the brain's nerve pathways after just a few cigarettes, suggesting that even a limited exposure to nicotine may initiate the addiction process (Mansvelder, Keath, & McGehee, 2002). This might explain why 94% of those children who smoke just four cigarettes go on to smoke regularly (Mansvelder et al., 2002). Still, up to 33% of smokers may not be addicted, as evidenced by a non-daily need to smoke, and just smoke occasionally (Kalman et al., 2015; Mansvelder et al., 2002). These people are classified as “**chippers**,” but unfortunately very little is known about this subgroup of individuals who smoke. Given the chipper's genetic heritage, he or she might be more or less vulnerable to the addictive effects of nicotine (Whitten, 2011), and it is possible that some persons identified as chippers are in the transitional phase between recreational use and full addiction to nicotine.

An estimated minimum of 66% of smokers are addicted to nicotine (Kalman et al., 2015), and demonstrate the characteristic symptoms of drug addiction: (1) tolerance, (2) a characteristic withdrawal syndrome, and (3) drug-seeking behaviors. Individuals who smoke cigarettes also (4) titrate their smoking to maintain a fairly constant level of nicotine in their blood (Oncken & George, 2005). When given cigarettes with a higher nicotine content, smokers will smoke less, while they increase the frequency of their cigarette use when given cigarettes with a lower nicotine content. Smokers of low-“tar” cigarettes have also been observed to inhale more deeply, and hold their breath longer, than do smokers of high-tar cigarettes. Smokers also develop individualized smoking rituals, which seem to provide them with a sense of security and contribute to the urge to smoke when the individual is anxious.

Nicotine Withdrawal

Symptoms of withdrawal from nicotine typically begin within 2 hours of the person's last cigarette, peak within 24 hours (Oncken & George, 2005), and then gradually decline in intensity over the next 10 days. The exact nature of nicotine withdrawal varies from individual to individual, and in spite of the horror stories often told about nicotine withdrawal, approximately a quarter of those who smoke report no significant withdrawal distress when they quit smoking. The reported symptoms of nicotine withdrawal include sleep problems, irritability, impatience, difficulty in concentration, lightheadedness, restlessness, fatigue, drowsiness, strong craving for tobacco, hunger, gastrointestinal

¹¹See Glossary.

¹²Leamon, Wright, and Myrick (2008) suggested that one-third of those persons who smoke just one cigarette will go on to become addicted to nicotine.

upset, constipation, headache, and increased coughing. Extended withdrawal symptoms appear to continue for as long as six months after the individual's last cigarette, although they vary in intensity from one person to another. Although many individuals report that smoking helps them to calm down, there is strong evidence that cigarette smoking can induce or exacerbate anxiety symptoms in those individuals with a panic disorder (Isensee, Hans-Ulrich, Stein, Hofler, & Lieb, 2003).

Complications of Long-Term Use of Tobacco Products

Those who smoke cigars and pipes and people who chew tobacco are only a small percentage of individuals who use tobacco. While chewing tobacco and pipe or cigar smoking carry many of the same health risks associated with cigarette smoking (Rodriguez et al., 2010), cigarette smoking is considered both the most common form of tobacco use and the “most lethal delivery system” (Erickson, 2007, p. 133) possible. The tobacco industry as a whole might be said to have engaged in a long-standing battle to avoid acknowledging that it knew a great deal about the dangers of tobacco use for decades before finally admitting to the fact (Mukherjee, 2010). While many admit to being aware of the dangers associated with tobacco use, they also maintain an illusion of personal immunity from smoking-related problems, at least until they develop a smoking-related medical disorder (Rogers, 2008). To put the relative risk of premature death into perspective, the body of a person who smokes appears to be 5–10 years older than their chronological age (Woloshin, Schwartz, & Welch, 2008), and the typical male will lose 13.2 years of potential life and the average female 14.5 years of potential life as a result of smoking-induced illness (Carmona, 2004; Sundaram et al., 2004). This data is significant since the cost of smoking-related health care problems in the United States alone is estimated to be \$400 billion a year (George & Weinberger, 2008), with worldwide estimates at \$1.4 trillion (World Health Organization, 2017b). The health consequences of cigarette use appear to begin to manifest in middle adulthood: Individuals who do not smoke enjoy a better quality of life than do cigarette smokers after reaching middle adulthood (Strandberg et al., 2008).

Tobacco is thought to cause approximately 7 million deaths each year worldwide (World Health Organization, 2017b). This number includes nonsmokers who die each year as a result of “passive” or “secondhand” smoking (discussed later in this chapter). The top three causes of smoking-related deaths in the United States are cancer

(18,658 persons/year), cardiovascular disease (128,457 persons/year), and respiratory disease (392,683) (Lehne, 2013). There is some dispute in the United States as to the proportion of cancer-related deaths that are smoking-related. Ezzati, Henley, Lopez, and Thun (2005) suggested that 21% of all cancer deaths are smoking-related, although in some regions of the country where there is a strong tradition of smoking, this may be as high as 40%. The greatest proportion of smoking-related cancer deaths in the 30–74 age bracket are thought to be smoking-related and account for 74% of all cancer deaths (Leistikow, Kabit, Connolly, Clancy, & Alpert, 2008).¹³

Cigarette smoking can kill through a wide variety of conditions either caused or exacerbated by smoking. Nationally, cigarette smoking is thought to cause 17–30% of all deaths of cardiovascular disease, 24% of all deaths from pneumonia or influenza, and 10% of infant deaths each year (Burns, 2008; Hughes, 2005; Miller, 1999). However, the most common cause of death associated with cigarette smoking is cancer. There are regional differences in the proportion of deaths that are thought to be cancer-related around the world, in part because cigarettes manufactured in different countries contain different leaves prepared for smoking, which contain different combinations of the chemicals thought to contribute to the development of cancer (Ashley et al., 2010; Coghlan, 2009).

Smoking-related cancers are not limited to the lungs, and the proportions of other forms of cancer that are thought to be smoking-related are reviewed in Table 15-1.

Individuals who smoke cigarettes are more prone to have a higher incidence of kidney cancer as compared with those who do not smoke (Carmona, 2004). Although the relationship between cigarette smoking and cancer has been well documented, the causal mechanism has not been isolated.

TABLE 15-1 Proportions of Cancer Cases Associated with Smoking

Lung cancer	87%
Esophageal cancer	75%
Bladder cancer	30–50%
Pancreatic cancer	30%

SOURCES: Bacher et al. (2010); Freedman, Silverman, Hollenbeck, Schatzkin, and Abnet (2011); Hymowitz (2005); World Health Organization (2006).

¹³The difference between the conclusions reached by these two research teams is explained by the fact that Ezzati et al. (2005) examined all cancer-related deaths across the lifespan, while Leistikow et al. (2008) focused only on the 30–74 age group, persons who are most likely to develop smoking-related cancers.

There are known carcinogenic chemicals in cigarette smoke, and abnormalities in the bronchial cells have been found in 98% of current smokers, as compared to just 26% of non-smokers (Wadland & Ferencich, 2004). It has been suggested that one or more compounds in cigarette smoke are capable of causing damage to cellular DNA in the lungs, and the team of Lee and colleagues (2010) uncovered evidence of 50,000 genetic mutations in the body of a 51-year-old individual who had smoked approximately one and a quarter packs of cigarettes per day¹⁴ for the preceding 15 years. Such genetic mutations might be the reason for the association between cigarette smoking and breast cancer, although the mechanism for this relationship is not clear. Guo and colleagues (2008) postulated that nicotine, even the reduced levels of nicotine found in secondhand smoke, interacted with receptors in breast tissue cells, signaling the cells to begin uncontrolled replication and migration.

The Mouth, Throat, and Pulmonary System

Individuals who smoke cigarettes are at increased risk for respiratory disorders during sleep, such as snoring and obstructive sleep apnea. The person who smokes is also 10–15 times as likely to develop lung cancer compared to the person who does not smoke (Kuper, Boffetta, & Adami, 2002). Those who smoke are also thought to be 27 times more likely to develop laryngeal cancer than nonsmokers, and the risk for these forms of cancer is dose-related (World Health Organization, 2006). Those who smoke are also at increased risk for chronic bronchitis, pneumonia, and chronic obstructive pulmonary disease (COPD) (Brust, 2004). Surprisingly, only about one-third of patients tested were aware that they had COPD, a condition found in about 20% of individuals who smoke cigarettes (Hill et al., 2010). It has been estimated that 80–90% of the deaths from COPD might be traced to cigarette smoking (Anczak & Nogler, 2003).

The individual's vulnerability for developing COPD is based in part on their genetic heritage; however, once it develops, it is a potentially fatal complication for smokers who continue to smoke (Sadeghejad et al., 2009). Ten percent of those individuals over the age of 65 who manifest COPD symptoms continue to smoke (Gwinnell & Adamec, 2006). It is not uncommon for these persons to rationalize their continued smoking saying that, since the damage has already been done, there is no sense in quitting cigarettes. In reality, there are benefits to quitting, even for the elderly. For example, 3 months after quitting cigarettes,

lung function will have improved by about one-third, which is a matter of importance for patients with COPD (Gwinnell & Adamec, 2006).

The Digestive System

Cigarette smoking is the cause of approximately half of all cases of gum disease and tooth loss (Centers for Disease Control, 2004). As noted earlier, individuals who smoke are also at increased risk of developing cancer of the mouth or throat. This effect is multiplied if the smoker is also a heavy drinker. Where those who smoke heavily have been found to have a seven-fold higher incidence of cancer of the mouth and pharynx than nonsmokers, and those who drink heavily have a six-fold higher incidence of these forms of cancer, the individual who smokes heavily and drinks heavily has a 38-fold higher incidence of cancer of mouth and pharynx ("Alcohol and tobacco," 1998).

Cigarette smoking contributes to the formation of gastric ulcers, especially peptic ulcers, and cancer of the stomach, and is a factor in the development of some forms of cancer of the pancreas (Carmona, 2004). For reasons that are not understood, those who smoke are also at increased risk for the development of type 2 diabetes (Willi, Bodenmann, Ghali, Faris, & Cornuz, 2007; Yeh, Duncan, Schmidt, Wang, & Brancati, 2010). The reason for this association is not known, although lifestyle factors such as a lack of exercise and poor diet are possibilities, and the increased risk for type 2 diabetes does not appear to decrease with smoking cessation (Yeh et al., 2010).

The Cardiovascular System

Cigarette smoking has been identified as the leading risk factor for heart disease, which results in a death every minute in the United States (Committee on Secondhand Smoke Exposure and Acute Coronary Events, 2009). Cigarette smoking is thought to account for approximately 30% of these deaths. The mechanisms by which cigarette smoking contributes to deaths from cardiovascular disease are varied. Smoking even a single cigarette has been shown to alter cardiac rhythm (McClain, 2006). In addition, the coronary arteries briefly constrict when a person smokes. Since the coronary arteries are the main source of oxygen and nutrients to the heart, anything that causes even a transitory constriction of the coronary arteries is a matter of concern. If the artery is also partially blocked by atherosclerotic plaque, the reduction in blood flow might be so severe that parts of the heart muscle begin to die for want of oxygen and nutrients. Heart attack survivors who continue to smoke are at increased risk for a second heart attack, bringing with it the risk of premature

¹⁴Often abbreviated as *ppd*.

death from heart disease. This risk can be reduced by a reduction in cigarette use: If the person were to cut back just five cigarettes per day they would reduce their chances of premature mortality by 18% (Gerber et al., 2009). If the individual should quit smoking after having the first heart attack, their risk of experiencing a second heart attack begins to drop within 6–12 months of his or her last cigarette.

Individuals who smoke cigarettes have been found to be at increased risk for hypertension,¹⁵ the development of aortic aneurysms, and atherosclerotic peripheral vascular disease. Those who smoke are also at increased risk for strokes, contributing to the 26,000 fatal strokes each year in the United States (Carpenter, 2001). Further, cigarette smoking introduces large amounts of carbon monoxide into the blood, blocking its ability to carry oxygen to the body tissues. The blood of a person who smokes cigarettes might lose as much as 15% of its oxygen-carrying potential as smoking-induced carbon monoxide binds to the hemoglobin in the blood (Parrott, Morinan, Moss, & Scholey, 2004; Tresch & Aronow, 1996).

The Skin

Smoking has long been associated with a skin condition known as “premature aging” (Parrott et al., 2004). Drawing on the data obtained from a research sample of 82 subjects aged 22–91, the team of Helfrich and colleagues (2007), attempted to develop an objective scale to assess adult skin aging. They found that cigarette smoking was associated with a dose-related premature aging of the skin of the face, as expected, but also found that this premature aging process involved the entire skin, not just the skin of the face, as had long been believed.

The Central Nervous System

There is an emerging body of evidence that a compound known as NNK,¹⁶ a carcinogen found only in tobacco, appears to cause the release of proteins that contribute to inflammation, as well as damage to the neurons of the brain (Ghosh et al., 2009). The possibility that a similar process might cause brain damage in humans who smoke cigarettes has not been confirmed or ruled out. There is, however, strong evidence that smoking might speed up the progression of damage seen in multiple sclerosis, although this is still uncertain because of conflicting research findings (Healy et al., 2009). After periods of debate and

contradictory research findings, cigarette smoking has been accepted as a risk factor for at least some forms of amyotrophic lateral sclerosis (ALS) (Armon, 2009).

The Reproductive System

The impact of cigarette smoking on women’s health is discussed in detail in Chapter 18. It is sufficient to point out here that cigarette smoking interferes with the normal function of women’s reproductive system. Males who smoke are at increased risk for various reproductive system problems, including smoking-related erectile dysfunction (Wen, Rissell, Cheng, Richters, & de Visser, 2017). The causal mechanism for this might be cigarette-related vascular damage to the blood vessels involved in the erectile response (Bach, Wincze, & Barlow, 2001). Surprisingly, while cigarette smoking does not appear to raise the individual’s risk for cancer of the prostate, men who smoke appear to have a higher *mortality rate* from prostate cancer than nonsmokers, for unknown reasons (Carmona, 2004).

Other Complications Associated with Cigarette Smoking

For reasons that remain unclear, cigarette smoking is thought to cause, or at least exacerbate, psoriasis. There is also strong evidence that cigarette smoking might exacerbate rheumatoid arthritis in persons with the genetic predisposition for this disorder (Lundstrom et al., 2009). There is also an apparent relationship between cigarette smoking and bone density loss in postmenopausal women (Carmona, 2004). In addition, there is preliminary evidence suggesting that cigarette smoking can speed up the progression of HIV infection¹⁷ (Lezak, Howieson, Bingler, & Tranel, 2012). Smoking appears to be related to a higher incidence of cataract formation, although the causal mechanism is not clear at this time (Centers for Disease Control, 2004). Individuals who smoke cigarettes also appear to be at higher risk for the development of macular degeneration (Tan et al., 2008).

Those who smoke cigarettes are twice as likely to have suicidal thoughts as are nonsmokers the same age (Bronisch, Hofler, & Lieb, 2008). This may or may not be associated with the altered brain function in those who formerly smoked, which continues for an extended period of time after the smoker’s last cigarette. Many individuals who used to smoke will report that they “never felt quite right” after they gave up cigarettes. There is evidence suggesting that there is a decline in cognitive abilities in middle-aged smokers that

¹⁵Itself a known risk factor for stroke.

¹⁶If you must know: 4-methylnitrosamino-1-(3-pyridyl)-1-butanone.

¹⁷Discussed in Chapter 36.

might linger for many years after the individual's last cigarette (Moon, 2008a). On the basis of their research, Dregan, Stewart, and Guilloford (2012) concluded that smoking contributed more to cognitive decline than does hypertension. Although the authors stopped short of stating that cigarette smoking could lead to outright dementia, persons with multiple risk factors such as hypertension and diabetes plus smoking were at higher risk for a cognitive decline.

A surprising complication of cigarette smoking is what Cutler-Triggs, Fryer, Miyoshi, and Weitzman (2008) termed "food insecurity," or the inability to obtain sufficient supplies of food. There are an estimated 13 million children in the United States who grow up in homes where there are not always sufficient levels of food, and the authors found that 17% of those children who had at least one smoking parent could be classified as living in such a home, as opposed to just 9% of those children who were living in a home where the parents did not smoke. It was noted that in some families up to 20% of the family income was spent on tobacco rather than on other products such as food, according to the authors. This drain on the familial income then contributes to a reduction in food availability, which in turn can contribute to nutrition-based developmental problems for the child.

Early studies suggested that cigarette smoking might provide some protection against the later development of Alzheimer's disease. Subsequent research failed to support the initial study, and subsequent research has suggested that those who smoke might be at *increased risk* for the development of Alzheimer's disease, vascular dementia, and general cognitive decline later in life (Lezak et al., 2012; Sundaram et al., 2004). Surprisingly, there is statistical evidence that those who smoke cigarettes have a 59% *lower risk* for a rare type of brain tumor known as acoustic neuroma (Palmisano et al., 2012). The authors hypothesized that the reduced blood flow caused by cigarette smoking might be a factor in this lower risk for such tumors. However, such tumors are so rare that the risks of smoking-related disease far outweigh any benefit in acoustic neuroma growth for the individual.

Smoking also results in indirect economic loss each year in the United States. For example, smoking is suspected of being a factor in the estimated 900,000 fires that fire departments respond to each year, and \$621 million in property damage, along with more than 2,000 injuries or deaths (Hall, 2013). These figures are not inclusive, but do suggest that the economic drain brought on by tobacco use is significant.

Additives

It should be noted that the information about the adverse effects of tobacco use discussed thus far involves *just tobacco*. Recent revelations based on classified documents

released as part of litigation against a major tobacco company (Phillip Morris) revealed evidence that their research into the safety of some 333 additives such as menthol was subjected to changes in research protocols or the statistical analysis after the conclusion of the study (apparently to minimize evidence of adverse effects of an additive(s)) (Wertz, Kyriass, Paranjape, & Glantz, 2011). There is further evidence suggesting that research protocols were designed by at least the one tobacco company identified in the research papers released in the litigation in such a way as to minimize the odds of adverse effects being identified (Wertz et al., 2011).¹⁸ Thus, the reader should keep in mind the fact that additives to cigarettes pose health risks in their own right. For example, Vozoris (2012) suggested that individuals who used a mentholated brand of cigarettes were at higher risk for a stroke than were those who smoked but did not use such cigarettes.

Degrees of Risk

There is no such thing as a "safe" cigarette. Although the tobacco industry claims that it is attempting to find or develop a safer cigarette, "The search for a safer cigarette is akin to alchemists seeking to turn lead into gold" (Blum, 2008, p. 1646). Even smoking just a few cigarettes a day carries with it an increased risk for smoking-related medical problems, and smoking cessation is the only known way to reduce these risks (Carmona, 2004). "Low-tar" or "light" cigarettes appear to offer the same degree of risk as regular cigarettes (Carmona, 2004). Smoking as few as three cigarettes a day has been found to increase the individual's risk of cardiovascular disease by 65% (Pope et al., 2009). Further, the concurrent use of cigarettes, smokeless tobacco, and snuff increases the individual's risk for smoking-related illness even further (Thorne, McClave, Rock, Asman, & Malarcher, 2010).

Smokeless Tobacco

There are multiple types of "smokeless" tobacco in use today: (a) moist "snuff," (b) dry snuff, (c) chewing tobacco (often called "spit tobacco"), (d) snus (moist tobacco powder), and (e) the newly introduced dissolvable tobacco. In the United States, only an estimated 3.4% of those who use tobacco (or 9 million people) use "smokeless" tobacco products (SAM-HSA, 2016). Generally, the use of chewing tobacco starts between the ages of 13 and 17, although those who have

¹⁸For example, using only 15 experimental animals rather than say 100, or setting the parameters of the study so that it was terminated in 60 days, thus preventing the cumulative effects of the compound(s) under study from developing.

been using cigarettes and who are trying to quit might substitute the use of chewing tobacco for their cigarettes. These individuals represent a subpopulation of those who use smokeless tobacco, and they tend to be older at age of initiation than the typical individual who uses smokeless tobacco.

The use of smokeless tobacco predominantly involves men, although a small percentage of women (0.6%) do use these forms of tobacco (Maldonado, 2010; SAMHSA, 2016). Many of these people use smokeless tobacco on the assumption that it is safer and exposes them to lower levels of nicotine than smoked tobacco. Unfortunately, research has demonstrated that using chewing tobacco 8–10 times a day will result in blood levels of nicotine similar to those seen in a one-and-a-half- to two-pack-per-day cigarette smoker (Shipley & Rose, 2003). Further, some of the compounds found in chewing tobacco have been linked to hypertension, and there are at least 16 carcinogenic compounds in the typical sample of chewing tobacco (Hecht & Hatsukami, 2005). This places those who use smokeless tobacco at increased risk for cancer of the mouth and throat (Hecht & Hatsukami, 2005). Indeed, the team of Hecht and colleagues (2007) found *higher* levels of one known carcinogen¹⁹ in the urine of those who used smokeless tobacco than was found in the urine of those who smoked cigarettes.

Further, recent research shows that those who use smokeless tobacco are at *higher* risk for a fatal myocardial infarction and/or stroke than are those who smoke cigarettes, and that it is of questionable value in smoking cessation programs (Boffetta & Straif, 2009; Piano et al., 2010). This might reflect smokeless tobacco's ability to increase heart rate and blood pressure (Boffetta & Straif, 2009). Those who use "chewing" tobacco also have a higher risk of cancer of the pancreas as well as a higher risk of oral and throat cancers (Boffetta, Hecht, Gray, Gupta, & Straif, 2008). Those who chew tobacco often experience problems controlling their blood pressure as well. Thus, while smokeless tobacco is often viewed as the "lesser of two evils" by those who use it, this product is certainly not without its risks.

Secondhand Smoke²⁰

It has been estimated that fully 1% of all deaths around the world can be attributed to individuals' exposure to secondhand smoke (Oberge, Jaakkola, Woodward, Peruga, & Pruss-Ustun, 2010). Clinically, this appears to make sense:

Nonsmokers who associate with those who smoke are exposed to many of the same toxins found in cigarette smoke. Research has found, for example, that the vast majority of *nonsmokers* tested positive for cotinine, a metabolite of nicotine, in their blood. This exposure to cigarette smoke is called "secondhand" or "environmental" smoke, and research has found that it presents significant danger to the nonsmoker.

There is strong evidence that the Tobacco industry tried to discredit research that associated exposure to secondhand or environmental tobacco smoke to heart diseases (Tong & Glantz, 2007). In spite of such denials, research has demonstrated that the coronary arteries of those exposed to secondhand smoke experience short-term coronary artery constriction after their exposure to cigarette smoke, just as do those who smoke cigarettes (Gullu et al., 2007; Otsuka et al., 2001). Unfortunately, few persons admitted to a coronary care unit are asked about possible exposure to environmental tobacco smoke to identify a potential risk factor for the individual's heart problem (Wilson, Shannon, & Shields, 2017).

Exposure to environmental tobacco smoke is thought to speed the formation of atherosclerotic plaque by 20% in persons exposed to environmental tobacco smoke, as opposed to 50% faster for the individual actively smoking. The association between environmental tobacco smoke and heart disease is so strong that Hurt and colleagues (2012) advised that persons with known coronary artery disease avoid *all* exposure to secondhand smoke, if possible.

There is a growing body of evidence that extended exposure to environmental tobacco smoke increases the individual's risk of an initial, and, if the individual survives, subsequent myocardial infarctions. When the team of Pell and colleagues (2008) examined the hospital admission records of nine hospitals in Scotland after a law was passed banning cigarette smoking in bars, restaurants, and other public places, they discovered that the number of admissions to these hospitals for acute coronary syndrome dropped 17% in the first year following the start of the ban. This is a significant and not isolated measure of the contribution of secondhand smoke to heart disease. The team of Meyers, Neuberger, and He (2009) also concluded that the risk of acute myocardial infarction drops by 17% in the first year of a public smoking ban, and in the city of Pueblo, Colorado, hospital admissions for acute myocardial infarctions dropped by 41% after implementation of smoking ban in public places ("Reduced hospitalizations for acute myocardial infarction," 2008). Additionally, the team of Hurt and colleagues (2012) found a 33% reduction in hospital admissions for myocardial infarction as well as a 17% decrease in sudden cardiac deaths following implementation of a ban on smoking in restaurants and other workplaces in Olmstead County, Minnesota.

¹⁹Which was the compound 4-(methylnitrocamino)-1-(3pyridyl)-1-butanol and its metabolites.

²⁰Also called *passive smoking* or *environmental tobacco smoke*. All three terms will be used in this chapter.

Individuals who are not smokers but who are exposed to significant amounts of environmental tobacco smoke are at greater risk for developing pulmonary disorders such as lung cancer or tuberculosis (Leung et al., 2010). Between 3,000 and 8,000 individuals who do not smoke die each year from cancer induced by environmental tobacco smoke just in the United States (Fiore, 2006). An interesting test of the theory that environmental tobacco smoke exposure could cause disease in those who do not smoke was carried out by Stark and colleagues (2007). The authors compared data from a sample of 52 restaurant workers who did not smoke but who worked at bars where smoking was permitted against 32 individuals who did not smoke and who worked at bars where smoking was prohibited. They found that the former group had six times the level of the compound NNAL²¹ in their urine as did those who worked at bars where smoking was not permitted. The importance of this study is that both sample groups were individuals who did not smoke, and NNAL is a smoking-specific carcinogenic compound, thus suggesting that those working in smoking-permitted bars were receiving significant exposure to toxic environmental tobacco smoke.

Adults who are exposed to secondhand smoke are also at higher risk for cognitive impairment than are those who are not exposed to cigarette smoke (Llewellyn, Lang, Langa, Naughton, & Matthews, 2009). The authors found that those adults with the highest level of exposure to environmental tobacco smoke were more likely to fall in the lowest 10% of cognitive testing, as compared with adults with lower levels of exposure to environmental tobacco smoke. Further, there is preliminary evidence that exposure to environmental tobacco smoke is associated with higher levels of mental health problems than for those not exposed to secondhand smoke, although the causal mechanism for this association is not known at the present time (Hamer, Stamatakis, & Batty, 2010).

Children are also vulnerable to environmental tobacco smoke and often do not have the choice to remove themselves from exposure, as some adults do. Researchers believe that secondhand smoke causes approximately 6,100 deaths in children each year in the United States. For example, children exposed to environmental tobacco smoke are at increased risk for developing asthma, which may be fatal if medical assistance does not arrive in time (Guilbert & Krawiec, 2003). The team of Kwok and colleagues (2008) concluded that for infants, the exposure to secondhand smoke in the first 3 months of life were twice as likely to develop an infectious disease(s), some of which were severe enough to require hospitalization, during the first 8 years of their lives. Another

measure of the vulnerability of children to environmental tobacco smoke was provided by Kerrigan (2008), who utilized data from the state of Wisconsin infant follow-up studies, and suggested that 56% of those infants who died after discharge from the hospital following birth had been exposed to environmental tobacco smoke.

Childhood exposure to secondhand smoke is an apparent risk factor in the later development of pulmonary diseases such as emphysema (Lavas et al., 2010) or lung cancer (Oliva-Marston et al., 2009) for the individual later in life. Lovasi and colleagues (2010) hypothesized that early damage to the alveolar walls might increase the child's chances of developing emphysema in middle to late adulthood. However, while the results of these studies are suggestive, they are not proof that such relationships exist, and there is a need for further research into childhood exposure to secondhand smoke and adult pulmonary disease. As these studies and those cited in earlier paragraphs suggest, environmental tobacco smoke is a serious health risk for those who are around the individual who smokes, and a factor in premature illness or death for a significant number of infants or children who were in effect involuntarily smoking.

It has even been suggested that exposure to tertiary, or "third-hand" tobacco smoke could be harmful, although this claim is controversial (Robson, 2009). Tertiary tobacco smoke exposure occurs when the individual who does not smoke is exposed to the residue of cigarette smoking found in the dust on clothing and environmental surfaces. However, the scientific validity of such claims has been challenged, not by the tobacco industry but by a small group of independent scientists (Robson, 2009). Nonetheless, the World Health Organization (2017b) concluded that third-hand smoke should continue to be investigated for its impact on global health and the environment.

Recent research has suggested that in the past "big tobacco" paid scientists to write articles contradicting the research suggesting that smoking was dangerous.²² They remain mute about the fact that many scientists conducting research into the dangers of cigarette smoking receive funding from companies that make nicotine replacement products (Robson, 2009). This is not to imply that cigarette smoking, or environmental tobacco smoke, are not dangerous. It does, however, underscore the need for a careful, *unbiased*

²¹Chemical shorthand for 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol.

²²An interesting phenomenon is the so-called Tobacco Research Institute, which purports to conduct unbiased research into tobacco and its uses. It is funded by "donations" from each tobacco company, which are assessed on the basis of the total market share that company holds (Pennock, 2007). However, fully 50% of the budget for this organization is devoted to public relations activities, a most curious application of research funds. Further, it continues to devote much of its activity to debunking research that suggests that tobacco smoking is dangerous.

examination of the evidence before claims of danger, or the extent of such danger, from either direct or indirect exposure to cigarette smoke are made.

Smoking Cessation

The most effective treatment for nicotine addiction is for the individual never to begin using tobacco products. To this end, some nations now require graphic warning labels on the side of the cigarette package illustrating the potential danger(s) of smoking. It has been found that clear, graphic images of the dangers inherent in tobacco use prominently displayed for the individuals who smoke to see increases the percentage of these individuals who contemplate smoking cessation, and improves their motivation to complete this task ("Cigarette package health warnings and interest in quitting smoking—14 countries, 2008–2010," 2011).

Admittedly, those who formerly smoked continue to have a higher risk for various forms of disease than individuals who never smoked. Pirie, Peto, Reeves, Green, and Beral (2012) found, for example, that those who smoked in the past were at one-third increased risk for premature death from smoking-related illness than those who never smoked. This was especially true for those who quit at the age of 50, suggesting that those who stop smoking at a younger age might be at lower risk for death from smoking-related illness. While the fact that women in the study who quit smoking still had a 33% higher risk of mortality from smoking-related illness might be used by some individuals to justify continued cigarette use, smoking cessation by the age of 50 still reduced the individual's risk of premature death from smoking-related illness by two-thirds, which is hardly insignificant.

Around half of individuals who smoke cigarettes try to quit in any given year (Kalman et al., 2015). Admittedly, it is difficult to quit smoking, and only 4–7% of individuals who smoke are able to quit without assistance in a given year (Sepe, Kay, & Stober, 2012). Between 70 and 80% of those who attempt to quit will relapse in the first 6 months, and typically will require 5–10 serious attempts to quit smoking before achieving success. However, success is possible, as evidenced by the fact that there are more people who used to smoke in the United States today than those who currently smoke (Fiore, Hatsukami, & Baker, 2002; Hays et al., 2011; Hughes, 2005), and eventually 30% of individuals who smoke cigarettes do quit, while an unknown percentage reduce their level of tobacco use (Lehne, 2013). Those who smoke 20 cigarettes a day or fewer appear to be more capable of stopping on their own, while those who smoke more heavily are more likely to require professional assistance.

In spite of public media advertisements suggesting that individuals who smoke require pharmacological support to quit, between two-thirds and three-quarters of those who previously smoked were able to quit without pharmacological support, and found that quitting was easier than they had anticipated (Chapman & MacKenzie, 2010). However, little is understood about the smoking cessation process. There is strong evidence, for example, suggesting that the individual's dietary choices might influence his or her success in quitting. The team of McClemon, Westma, Rose, and Lutz (2007) found that individuals who consumed meat, coffee, and alcohol experienced greater pleasure from cigarette use, while foods such as dairy products, celery, and other vegetables reduced the sense of pleasure from smoking. Thus, those who wish to quit smoking must review their dietary habits and change their diet to give themselves the best possible chance of quitting.

The most common, and possibly least effective, method of smoking cessation is the "cold turkey" method, in which the smoker just quits smoking (Patkar, Vergare, Batka, Weinstein, & Leone, 2003). The sudden discontinuation of cigarettes tends to result in high relapse rates, as opposed to those methods of smoking cessation that utilize a nicotine replacement component and psychosocial support (Patkar et al., 2003). The various pharmacological supports for smoking cessation are reviewed in Chapter 33.

Individuals who smoked in the past are vulnerable to "relapse triggers" that they encounter in the environment, the most important of which is being around people who are still smoking. Watching others smoke cigarettes, and smelling tobacco smoke from a distance, will trigger thoughts of returning to active smoking for the individual. Another relapse trigger is living in a home with more than one individual who smokes. These relapse triggers are a factor in more than 50% of cases where the individual who previously smoked relapses (Ciraulo, Piechniczek-Buczek, & Iscan, 2003). Thus, like other forms of SUDs, the individual in recovery must change friendships, avoid high-risk situations, and be aware that environmental triggers will make him or her think about smoking.

There is a poorly understood relationship between depression and cigarette smoking. Evidence suggests that individuals who smoke and who are also depressed experience more reinforcement from cigarettes than do those who are not depressed, and they are vulnerable to possible relapse because of this (Patkar et al., 2003). This is not to say that cigarette smoking causes the depression. Rather, depression and cigarette smoking appear to be two separate conditions that overlap, with depression possibly serving as a relapse trigger for those who are in recovery. Other emotional states, such as boredom or anxiety, can also serve as relapse triggers, as many people have learned to cope with these emotions through smoking.

It is also important for clinicians to realize that severe nicotine withdrawal may cause symptoms that could be misconstrued as other psychiatric disorders (Kalman et al., 2015).

Cigarette Cessation and Weight Gain

Many smokers cite their fear of gaining weight as an obstacle to smoking cessation. Admittedly, about 80% of individuals who quit smoking will gain *some* weight in the early stages of recovery (Centers for Disease Control, 2004). However, this statistic is misleading: 57% of those who continue to smoke also gain weight during the same period of life, suggesting that some of the weight gain might be falsely attributed to smoking cessation rather than just a tendency on the part of the person who smokes to gain weight as he or she ages. Still, individuals in the early stages of smoking cessation do need to watch their diets. The average individual who is quitting smoking increases his or her caloric intake by about 200 calories a day, the equivalent of about one sandwich per day (Stitzer, 2003). Over the course of a week, the extra accumulated caloric intake would amount to 1,400 calories, which means that the person would be ingesting 8 days' worth of calories every 7 days. This obviously will expose the individual to the danger of weight gain, at least in the short term.

Another factor that contributes to weight gain in the individual who quits smoking is that nicotine stimulates the body's metabolism by about 10%, forcing the body to "burn" calories faster than normal (Stitzer, 2003). Finally, many people who smoke are underweight because of nicotine-induced anorexia. When they stop smoking, their bodies will attempt to "catch up" and add weight to achieve the individual's appropriate weight level for his or her body frame. Finally, those who smoke are often fluid-deficient, and when they stop smoking the body will ingest extra fluids to achieve the appropriate fluid levels. These factors may contribute to cessation-related weight gain in the individual who quits smoking.

Clinicians often underestimate the amount of weight gained by a person who quits cigarette smoking following cessation. Aubin, Farley, Lycett, Lahmek, and Aveyard (2012), who suggested the average person who quits would gain weight over time (see Table 15-2). Surprisingly, there

is evidence suggesting that those individuals who gain more weight are also more likely to abstain from cigarettes. Further, although this weight gain is often distressing to the individual, there is evidence that after 6 months or so the average individual's body weight will return to precessation levels. Thus, cessation-related weight gain may be a transitional step in the person's adjustment to life without cigarettes.

While obesity is a known risk factor for cardiovascular disease, the health benefits that accrue from smoking cessation usually far outweigh the potential risks from cessation-related weight gain (Clair et al., 2013). A person who used to smoke would need to gain 50–100 pounds to place the same stress on her or his cardiovascular system as they did by smoking one to two packs a day. Thus, post-cessation weight gain is not as dangerous as continued cigarette smoking. Table 15-3 lists some of the benefits of smoking cessation.

TABLE 15-3 Summary of Benefits of Smoking Cessation

Condition	Benefit
Stroke	Within 5–15 years, the individuals risk of stroke will be about the same as that of a person who never smoked.
Cancer of the mouth, throat, and the esophagus	After 5 years of abstinence the individual's risk of developing one of these cancers drops 50%.
Coronary artery disease	After 1 year of abstinence the individual's risk of coronary artery disease drops by 50%. After 15 years of abstinence it will be virtually the same as for someone who never smoked.
Lung cancer	The risk of lung cancer will drop 50% in first 10 years of smoking abstinence.
Hypertension	Drops as arterial walls become more flexible in first 10 years of abstinence from smoking.
Life expectancy	Quitting smoking adds between 2.5 and 4.5 years to their life expectancy.
Neurosurgery patients	Lower risk of complications or mortality during and after neurosurgical procedure.
Recovering cardiac patients	Individuals who no longer smoke are less likely to suffer a second heart attack compared with those who continue to smoke.

SOURCES: Centers for Disease Control (2004); Grover, Gray-Donald, Joseph, Abrahamowicz, and Coupal (1994); Lau, Berger, Khullar, and Maa (2013); Jatoti, Jerrard-Dunne, Feely, and Mahmud (2007).

TABLE 15-2 Weight Gain Following Smoking Cessation

Time Since Quitting	Weight Gain
1 month	2.46 pounds
2 months	4.97 pounds
3 months	6.27 pounds
6 months	9.3 pounds
12 months	10.27 pounds

Tobacco Use and the *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition)²³

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) identified four subforms of tobacco-related disorders:

1. Tobacco use disorder
2. Tobacco withdrawal
3. Other tobacco-induced disorders
4. *Unspecified tobacco-related disorder*

The DSM-5 (American Psychiatric Association, 2013) identified 11 criteria by which a tobacco use disorder might be identified, with individuals who demonstrate any two of these criteria in a 12-month period meeting the criteria for a diagnosis for a tobacco use disorder.²⁴ The identified criteria include (but are not limited to) (American Psychiatric Association, 2013) craving for tobacco when not being used, recurrent tobacco use in situations where its use is dangerous (smoking in bed was the example provided in the DSM-5), continued tobacco use even though one knows the physical and psychological dangers associated with its use, development of tolerance, and a characteristic withdrawal syndrome. As with other substance use disorders classified in the DSM-5, the tobacco use disorders are on a spectrum from mild moderate to severe, with modifiers such as in early or in sustained remission suggested where appropriate. Other modifiers include whether the individual was in a nicotine maintenance program, in which the nicotine withdrawal syndrome is blocked by the pharmaceuticals being used, or if the individual was in a controlled environment with limited or no access to tobacco products.

It is noted in the DSM-5 that smoking is related to a number of physical problems, most of which are discussed earlier in this chapter. Between 22 and 32% of individuals who smoke have another substance use or psychiatric disorder (American Psychiatric Association, 2013). It is also noted that there are cultural and educational factors that might predispose an individual to smoking cigarettes (American Psychiatric Association, 2013).

Within 24 hours of the individual's last cigarette use, he or she will begin the phase of tobacco withdrawal, the symptoms of which are reviewed in this chapter. The DSM-5 warns that the symptoms being observed must not be caused by another condition such as withdrawal from another compound being used, and states that the withdrawal process requires "clinically significant distress or impairment" (p. 575) for the individual, although, as noted in this chapter, a significant percentage of individuals who smoke report minimal to no distress during cigarette cessation. This would suggest a need for another category for persons going through nicotine withdrawal "with minor distress only," in the opinion of the author of your text.

The category *other tobacco-induced disorders* is applied to cases where the individual's tobacco use has contributed to another medical disorder (such as a sleep disorder, for example; American Psychiatric Association, 2013). Finally, the *unspecified tobacco-related disorder* category refers to individuals whose tobacco use has caused significant impairment in their physical health, occupational functioning, or familial life, but who do not meet the full criteria for a diagnosis of a *tobacco use disorder* (American Psychiatric Association, 2013).

Chapter Summary

Tobacco use, which was once limited to what European explorers would come to call the New World, was first introduced into Europe by explorers who learned the practice of smoking during their travels. Once the practice of smoking tobacco reached Europe, it spread rapidly in spite of rather draconian measures by authorities to try to stop its spread. By the end of the 19th century, tobacco chewing had become a common practice, while the concurrent development of machines that allowed for the rapid production of cigarettes allowed health providers to suggest cigarette smoking as a less offensive, and more sanitary, substitute for chewing tobacco.

In the time since its introduction into society, nicotine, the main psychoactive agent in tobacco, has been found to have an addiction potential similar to that of narcotics or cocaine. Significant numbers of people have become addicted to cigarettes, and each year 50% of individuals who smoke attempt to quit. Unfortunately, only a small percentage of these individuals are able to discontinue the use of cigarettes each time they attempt to quit. This is a testament to the addictive potential of nicotine, but also reflects the sad fact that the majority of those who smoke will continue to expose themselves to the dangers associated with tobacco use.

²³The material presented here is to illustrate the relationship between the alcohol use disorders and the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition). This material should not be interpreted as, nor should it be used as, a diagnostic manual.

²⁴The reader is referred to the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) for the full list of diagnostic criteria suggested by the American Psychiatric Association as signs of tobacco use disorder.



CHAPTER 16

Over-the-Counter¹ Analgesics

Unexpected Agents of Misuse and Danger

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 16.1** Understand the history of over-the-counter analgesics
 - 16.2** Understand the medical uses of over-the-counter analgesics
 - 16.3** Describe the normal dosages and effects of over-the-counter analgesics
 - 16.4** Comprehend the pharmacology of over-the-counter analgesics
 - 16.5** Understand the concern with over-the-counter analgesic overdoses
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Introduction

At first glance, the reader might question why the over-the-counter (OTC) analgesics are included in a book on substance misuse. These compounds do not induce a sense of euphoria and are not “recreational” drugs. Yet OTC analgesics are ubiquitous: Seventy percent of adults over the age of 65 take an OTC analgesic at least once a week (Stillman & Stillman, 2007). Further, many individuals who misuse drugs will also use an OTC analgesic, either during the period of active drug use or immediately after these periods of substance use, despite the fact that they are not innocuous compounds. Each year in the United States, 16,500 people die from OTC-induced reactions (Savage, Kirsh, & Passik, 2008; Stillman & Stillman, 2007). Even the OTC nonsteroidal anti-inflammatory (NSAID) compounds have been found to increase the risk of myocardial infarction and stroke, each of which can result in death (Gonzalez-Valcarcel et al., 2016; Trellet et al., 2011). While the substance rehabilitation professional should not recommend the use of such medications, it is imperative that they have at least a working knowledge of the side effects of these compounds and their potential for harm.

A Short History of the OTC Analgesics

Folk healers have long used various plants or extracts from different plants to treat disease, especially pain and fever. One such plant extract is the bark of the willow tree, which contains *salicin* (from the Latin word *salix*, which means willow) and has been used for pain relief

¹Over-the-counter medications are available without a prescription. Thus the term over-the-counter medications.

and relief from fever for more than 2,000 years (Jeffreys, 2004; Stimmel, 1997a). Around 2,400 years ago, the Greek physician Hippocrates recommended that patients experiencing mild levels of pain or fever, or women in labor, chew the bark of the willow tree. But the bitter taste, limited availability of the bark, and the inconsistent effects forced physicians of the era to turn to opium as an alternative.

Then in the 1880s the active agent of willow bark, salicin, was isolated and research into the effectiveness of this compound was started. Although promising as an analgesic, salicin was found to induce gastric distress. Chemists chanced upon salicylic acid, which had the same properties as its chemical cousin salicin but was easier to produce. However, salicylic acid, like salicin, was found to cause a great deal of gastric distress when used. So chemists continued their search for a compound with the advantages of salicin but without its harsh effects. In 1898, Bayer Pharmaceuticals introduced the compound acetylsalicylic acid, which they sold under the brand name *Aspirin*². Like salicin, aspirin was found to be effective in controlling mild to moderate levels of pain without the harsh gastrointestinal side effects seen when salicylic acid was used³ or the danger of addiction inherent in the use of narcotic analgesics.

Because of its multiple effects, aspirin⁴ has become the most frequently used medicinal compound in the world (International Aspirin Foundation [IAF], 2017). An estimated 100 billion doses of aspirin are produced around the world each year (IAF, 2017), a quarter of which is consumed just in the United States each year (Page, 2001). However, these figures belie aspirin's potential for harm: While its side effects are less intense than those of salicylic acid, it is still not totally innocuous. This is why pharmaceutical companies embarked on a search for compounds with the benefits of aspirin without its side effects. This resulted in the discovery of a class of compounds known as the *propionic acids*, which include the compounds naproxen and ibuprofen,⁵ as well as acetaminophen, which was introduced as an OTC analgesic in the 1950s. The term "acetaminophen" (also known as paracetamol outside the

United States) is a form of chemical shorthand for the compound *N-acetyl-para-aminophenol*. This compound was first isolated in 1878, and while it was recognized that it could lower fever, it was feared that acetaminophen had the same dangerous side effects as a close chemical cousin, para-aminophenol, so it remained a footnote in the chemistry textbooks until the early 1950s (Mann & Plummer, 1991). By that time, sufficient evidence had accumulated to show that acetaminophen was much safer than para-aminophenol and that it did not have the same potential for gastric distress found in aspirin. A massive advertising campaign followed the introduction of a brand name of acetaminophen, which placed emphasis on how this compound was not irritating to the stomach, as was aspirin. This advertising campaign, combined with a growing awareness of aspirin's potential for gastric distress, made it the most commonly used compound for fever control worldwide at the start of the 21st century (Sharma, 2003).

This is not to imply that acetaminophen has entirely replaced aspirin, as aspirin remains a popular OTC analgesic worldwide. Indeed, more than a century after its discovery, scientists continue to find new applications for aspirin, and it has been suggested that if it were to be discovered today it would be classified as a prescription-only medication. However, aspirin does present the user with various potential side effects, some of which are potentially deadly to the user.

The Origins of the Term NSAID

As is true for the adrenocortical steroids (endogenous compounds produced by the body in response to stress), aspirin and the propionic acid derivatives (such as ibuprofen and naproxen) have an anti-inflammatory effect. However, because these compounds have a different chemical structure than the adrenocortical steroids, they are classified as *nonsteroidal* anti-inflammatory drugs (NSAIDs). There are approximately 20 NSAIDs currently in the United States, although most are available only by prescription. The exceptions to this rule are aspirin and the propionic acid derivatives briefly discussed earlier. Other NSAIDs are the COX-2 inhibitors, which were introduced in the 1990s and have a short but controversial history thus far, to be discussed later in this chapter.

Medical Uses of the OTC Analgesics

Aspirin

Aspirin was first introduced in late 1897 by Felix Hoffman (IAF, 2017). Aspirin is able to reduce fever by causing the blood vessels in the peripheral regions of the body to dilate

²Aspirin is a member of a family of closely related compounds, many of which have analgesic, anti-inflammatory and antipyretic action. However, since all of these compounds are less powerful than aspirin, they will not be discussed further in this chapter.

³This does not mean that aspirin does *not* induce gastrointestinal distress, only that it is less likely to do so than its chemical cousins.

⁴The word "aspirin" is a historical accident, discussed in detail in Mann and Plummer's 1991 text. It is far too complex to be discussed in this chapter, but from this point on the word "aspirin" with a lowercase "a" will be used.

⁵Other compounds, such as ketoprofen, were also developed from the propionic acids, but will not be discussed further in this chapter because they usually require prescriptions.

and by encouraging sweating. While this effect will reduce fever, it does not reduce the body temperature below normal. Aspirin has also been found to interfere with the production of a family of compounds known as the **prostaglandins**⁶ (Wilson, Shannon, & Shields, 2011). In the closing decade of the 20th century it was discovered that regular low-dose aspirin reduces the incidence of myocardial infarctions (MIs)⁷ in both men and women (Berger et al., 2006; Buring & Ferrari, 2006; Chan et al., 2007; Ogawa et al., 2008) and that it is of value *during* a myocardial infarction. However, in some patients, such as in those who have rheumatoid arthritis, current research shows this protective effect against MIs is not seen (Durán, Peloquin, Zhang, & Felson, 2017). Paradoxically, extended periods of aspirin use at high dosage levels appear to *increase* the individual's risk for heart disease or strokes, through what are known as "microbleeds" (D'Arcy, 2007; Vernooij et al., 2009), and use at low doses in those with low risk of vascular issues may not be worth the risk of bleeding incidents (Casado-Arroyo, Lanás, & Brugada, 2016). Thus, the physician must weigh the benefits against the potential risks associated with aspirin use before suggesting it to a patient (Casado-Arroyo et al., 2016; Xiong & Kenedi, 2010).

There are several mechanisms through which aspirin use can reduce the individual's risk for an initial or subsequent myocardial infarction. Aspirin impacts blood levels of the *C-reactive proteins*, compounds that at high levels have been found to be associated with an increased risk of either a myocardial infarction, an occlusive stroke, or a blood clot that might block a vein (a venous thrombosis) (Schrör & Voelker, 2016). Another mechanism by which aspirin is thought to reduce the incidence of heart attack is through the inhibition of a form of prostaglandin known as *thromboxane A2*, which is found in blood (Schrör & Voelker, 2016). Thromboxane A2 is involved in the formation of blood clots (Hutchison, 2004; Jeffreys, 2004; Page, 2001). However, there is a great interindividual variation in the ability of low-dose aspirin to block thromboxane A2, and each individual's aspirin requirements should be assessed by a physician. Further, since blood platelets have a normal life span of 8–10 days, the body is constantly replacing old blood platelets with new ones, which have stores of thromboxane A2. Thus, it will be necessary for the individual to take aspirin at least every day, or possibly every other day, to provide the desired inhibition of blood clot formation.

There is an ongoing controversy in the medical field about whether some patients are resistant to the anti-thrombotic⁸ effects of aspirin. Some physicians argue that the "resistance" is due to medication noncompliance. Others argue that some individuals are indeed more resistant to aspirin's antithrombotic effects than are others for reasons such as concurrent diseases such as diabetes (Dalen, 2007; Halushka & Halushka, 2002; Krasopoulos, Brister, Beattie, & Buchanan, 2008). Yet a third theory was offered by the team of Smith and colleagues (2011), who suggested that incomplete or delayed absorption of aspirin might reduce its effectiveness. Enteric coated aspirin, designed to reduce gastric distress for the user, might result in reduced aspirin absorption, a matter of critical importance for those persons who must take aspirin to prevent the formation of blood clots, according to the authors. Also, interaction with other medications or OTCs (such as ibuprofen) may contribute to the ineffectiveness (Schrör & Voelker, 2016). This debate about aspirin resistance continues in the clinical literature, and there is no consensus within the medical community at this time.

Scientists have also found that low doses of aspirin are effective as an adjunctive treatment for a rare neurological disorder known as *transient ischemic attack* (TIA). Regular use of aspirin at low doses has been found to slow the rate of cognitive decline in women who are at high risk for cardiovascular disease (Kern, Skoog, Ostling, Kern, & Borjesson-Hanson, 2012). There is also an impressive body of evidence suggesting that regular low doses of aspirin might reduce the incidence and spread of colorectal cancer (Rothwell et al., 2010, 2012). This appears to also be true for hormone receptor-positive breast cancer (Terry et al., 2004). There is also preliminary evidence suggesting that regular low-dose aspirin use is associated with a lower incidence of esophageal cancer and ovarian cancer (Page, 2001), and possibly a form of skin cancer known as melanoma. Aspirin has been found to improve the blood flow to capillaries that feed the retina, thus inhibiting the development of diabetic retinopathy (Adler & Underwood, 2002; Roberts et al., 2002). Further, there is evidence that regular low-dose aspirin use slows the process by which the eye forms cataracts, and might protect the sensitive structures of the inner ear from damage during the normal aging process, or from certain medications (Coghlan, 2006a).

There is even evidence that salicylates, the family of compounds from which aspirin is derived, might be of value in treating type 2 diabetes (Rumore & Kim, 2010). The

⁶See Glossary.

⁷Also known as a heart attack.

⁸See **thrombosis** in Glossary.

authors point out that the ability of aspirin to inhibit the production of cyclooxygenase⁹ appears to be partially responsible for aspirin's ability to inhibit insulin resistance and thus improve blood glucose control. Unfortunately, to be effective in controlling type 2 diabetes, aspirin would need to be used at levels far above those normally used, placing the patient at risk for a multitude of potentially serious consequences (Rumore & Kim, 2010). Still, the early results of the research appeared promising. As this list of known and potential applications of aspirin suggests, this compound is far more potent than most people suspect.

Acetaminophen

There is some disagreement in the medical world as to whether acetaminophen should or should not be classified as an NSAID. Most researchers do not classify acetaminophen as such, although it is quite useful. It is as effective as aspirin in the control of fever related to colds (American Society of Health System Pharmacists, 2008). As an OTC analgesic, it is as potent as aspirin, and may be used to treat virtually every pain condition that aspirin does, except those induced by inflammation. Acetaminophen has no significant anti-inflammatory action.

The Propionic Acids

This class of these NSAID compounds includes ibuprofen, naproxen, and ketoprofen,¹⁰ all of which are available over the counter.¹¹ As a group, these compounds are about as effective as aspirin and can treat the same conditions. The anti-inflammatory action of these compounds makes them useful in treating rheumatoid arthritis, dysmenorrhea, gout, tendinitis, and bursitis, as well as headaches and the aches and discomfort of the common cold. When used with narcotic analgesics, scientists have found that the NSAIDs increase the analgesic potential of the latter compounds, allowing for a greater range of pain control without the need to increase the dosage of the narcotic. There is mixed evidence suggesting that the regular use of NSAIDs (including aspirin) may slow the progression of Alzheimer's disease and vascular dementia (Adler & Underwood, 2002; Oveisgharan & Hachinski, 2016; Veld et al., 2001; Vlad, Miller, Kowall, & Felson, 2008).

⁹Discussed later in this chapter.

¹⁰This compound will not be discussed in detail since it has only a small share of the over-the-counter analgesic market.

¹¹These were all prescription-only medications at first, but were introduced as over-the-counter analgesics in modified dosage form from the prescription form of these same compounds.

The NSAIDs all present the user with some risk of cardiovascular problems. This risk is thought to be lower when the patient uses ibuprofen or naproxen, but the cardiovascular risks cannot be avoided when these compounds are used (D'Arcy, 2007). Further, the NSAIDs all function as nonselective **cyclooxygenase**¹² inhibitors, presenting the user with both benefits and the potential for harm. This will be discussed later in this chapter.

Normal Dosage Levels of the OTC Analgesics

Aspirin

Although some people easily dismiss aspirin as an analgesic, a standard dose of two 325-mg aspirin tablets provides an analgesic effect equal to that of 50 mg of the narcotic analgesic meperidine (Demerol), 32 mg of codeine, a 50-mg oral dose of pentazocine (Talwin), or 65 mg of propoxyphene (Darvon) (McGuire, 1990). However, the optimal analgesic dose of aspirin is still being debated. There is a "ceiling" effect that is encountered at doses of around 1,000 mg every 4 hours, after which larger doses do not bring about any more analgesia but do increase the possibility of an adverse reaction. The normal adult oral dose of aspirin is 325–650 mg every 4 hours as needed for pain. Furthermore, it is recommended that aspirin should not be used on a continuous basis for more than 10 days by adults, or 5 days by children, except under a physician's orders.

ACETAMINOPHEN

The usual adult dose of acetaminophen is 325–650 mg every 4 hours as need for the control of pain (Wilson, Shannon, & Shields, 2017). Acetaminophen's analgesic and antipyretic¹³ effects are approximately the same as aspirin's. Like aspirin, acetaminophen has a ceiling effect of approximately 1,000 mg every 4 hours. It is recommended that the individual not use acetaminophen for longer than 10 days unless advised to do so by a physician. Use is cautioned in those who have an alcohol use disorder (Wilson et al., 2017).

Ibuprofen

In its OTC form, the recommended dose of ibuprofen is 200–400 mg every 4 hours for the control of pain. At these dosage levels, ibuprofen has an analgesic potential that is

¹²See Glossary.

¹³See Glossary.

equal to that of aspirin or acetaminophen. As a prescription medication, dosage levels of 400–800 mg three or four times a day are usual (Wilson et al., 2011). Four hundred milligrams every 4–6 hours up to a maximum of 3,200 mg in a 24-hour period of time is recommended for the control of mild to moderate levels of pain (Wilson et al., 2011).

Naproxen

As an OTC analgesic, patients are advised to take one tablet every 12 hours. Prescription dosage levels are somewhat higher than the OTC analgesic dosage levels, but the patient is still advised to take the medication only twice daily.

Pharmacology of OTC Analgesics

Before these compounds are used, the *cause* of the fever or pain should be identified, lest the OTC analgesic being used mask the appearance of a serious medical condition that could be treated. Further, the patient is warned to follow dosing instructions for the specific OTC analgesic to minimize the risk to his or her life.

Aspirin

Aspirin is well absorbed from the gastrointestinal tract after oral ingestion, either with food or on an empty stomach. If ingested with food all the aspirin is still absorbed, but it will take 5–10 times longer than if the patient ingested the aspirin on an empty stomach. The food provides a “buffering” effect that might help protect the stomach lining from aspirin-related irritation, but at the cost of slower absorption. To avoid aspirin-induced stomach irritation, it is often sold in combination with antacids or with an enteric coating. However, these also result in erratic absorption rates, possibly contributing to the patient’s pain (Wilson et al., 2011). Antacids also reduce the amount of aspirin that reaches the patient’s circulation by 30–70%, a matter of some concern for patients who wish to control some form of pain.

When taken on an empty stomach, the absorption of aspirin depends on the speed with which the tablet(s) crumble, allowing individual aspirin molecules to pass through the gastrointestinal tract into the circulation. Peak blood levels of aspirin are achieved between 15 (Wilson et al., 2011) and 60–120 minutes (Stimmel, 1997a) after a single dose. Between 80 and 90% of single dose of aspirin is bound to plasma proteins, providing a reservoir of aspirin that might slowly be released back into the user’s circulation over a period of time (Stimmel, 1997a). The therapeutic half-life of aspirin is 2–3 hours following a single dose, although this

may be increased to 8–15 hours when aspirin is used on a regular basis. It is rapidly biotransformed into water-soluble metabolites, which are then removed from the circulation and excreted in the urine. Only about 1% of a single dose of aspirin is excreted unchanged. Tolerance to the analgesic effects of aspirin develops only rarely (Stimmel, 1997a).

Unlike narcotic analgesics, which work mainly within the brain itself, aspirin appears to work both at the site of injury and in the hypothalamus. There is also evidence that it works at still-to-be-identified sites in the spinal cord. To understand how aspirin works at the site of injury, it is necessary to investigate the body’s response to injury. Every cell in the body contains a variety of chemicals, some of which alert the body to cellular injury and death. Some of these chemicals are *histamine*, *bradykinin*, and a group of chemicals known as the *prostaglandins*. Aspirin inhibits prostaglandin production, thus limiting the inflammation and pain that develops in response to cellular injury.

Unfortunately, prostaglandin production is necessary for the compound cyclooxygenase, which has two subtypes: COX-1 and COX-2. A third subtype, tentatively classified as COX-3, has been identified, although its role in the body is still unclear at this time. COX-1 is involved in normal cellular maintenance, especially in the stomach and kidneys. COX-2 is released only when body tissues are damaged, contributing to the inflammation response. Unfortunately, both forms share 60% of the same chemical structure, and it is through the shared elements of their chemistry that aspirin and the other NSAIDs act. Thus, the NSAIDs could be classified as nonselective COX inhibitors, which provides both a benefit (reducing COX-2 production) and a danger (reducing COX-1 production) for the patient (Stillman & Stillman, 2007). There is also evidence that COX-2 inhibition also reduces the body’s ability to produce an enzyme¹⁴ that has cardioprotective effects. This preliminary research has yet to be duplicated and verified, however.

The inhibition of COX-2 appears to be the mechanism through which aspirin appears to be able to limit the development of colorectal cancer (Baron et al., 2003; Kreeger, 2003). However, this only involves those forms of colorectal cancer that over-express COX-2, not all forms of colorectal cancer (Chan, Ogino, & Fuchs, 2007). The routine use of aspirin to protect against colorectal cancer was discouraged by Dube and colleagues (2007), who suggested that any potential benefit gained from the use of an NSAID such as aspirin is outweighed by the dangers associated with the use of these compounds.

¹⁴Prostacyclin, or PGI-2.

Researchers believe that ingestion of just one 325-mg aspirin tablet a day for an extended period of time provides a modest degree of protection against prostate and breast cancer, but the operational mechanisms by which these effects are achieved, and the risk/benefit ratio for regular aspirin use as a protection against these conditions have not been calculated (Jacobs et al., 2007).

Acetaminophen

Acetaminophen is easily administered orally in tablet, capsule, and liquid forms. It may also be administered as a rectal suppository. After oral ingestion, virtually 100% of a single dose is absorbed through the gastrointestinal tract (Wilson et al., 2017). The peak effects are achieved in between 30 and 120 minutes, and acetaminophen is extensively biotransformed by the liver before excretion, although small amounts are possibly found in the breast milk of a lactating mother (Wilson et al., 2017).

Acetaminophen is as potent as aspirin as an analgesic and antipyretic agent. However, acetaminophen is toxic to the liver, and doses greater than 4,000 mg a day or use for longer than 10 days are not recommended except under a physician's supervision. Also, individuals who are alcohol-dependent must not use acetaminophen except under the supervision of a physician, to avoid the danger of liver damage brought on by the concurrent use of these two compounds. However, unlike the NSAIDs, acetaminophen does not interfere with the normal clotting mechanism of the blood, nor does it typically induce an allergic reaction, as is possible with aspirin use. Scientists speculate that since acetaminophen is not an inhibitor of either COX-1 or COX-2, there must be another mechanism by which it functions as an analgesic. This has tentatively been identified as the "COX-3" enzyme, which (if it exists) is limited to the central nervous system (CNS). Thus, if acetaminophen does inhibit COX-3, it does so in a yet-to-be-discovered region of the brain. The mechanism by which acetaminophen is able to reduce fever is also unknown at this time.

Ibuprofen

Ibuprofen is usually administered orally, and about 80% of a single dose of ibuprofen is absorbed from the gastrointestinal tract. Peak plasma levels are achieved about 30–90 minutes after ingestion of a single dose, and the half-life is between 2 and 4 hours (Wilson et al., 2011). About 99% of ibuprofen molecules become protein-bound after absorption, providing a reservoir of ibuprofen that is slowly released back into the circulation over time. Ibuprofen is extensively biotransformed

prior to elimination, and its metabolites are mainly eliminated through the kidneys. A small amount of a dose of ibuprofen is eliminated through the bile. Like aspirin, ibuprofen is a nonselective cyclooxygenase inhibitor. However, this is not to imply that it can automatically be substituted for aspirin in the control of inflammation. It requires 2–4 weeks of regular use before the full anti-inflammatory effects of ibuprofen are seen, and even then only if the individual is taking 2,400 mg a day or more. At this dosage level, it is about as effective an anti-inflammatory agent as aspirin. Unfortunately, one cannot take both aspirin and ibuprofen for control of inflammation, as the effects of one compound interfere with the anti-inflammatory effects of the other.

Ibuprofen is about one-fifth to one-half as irritating to the stomach as aspirin. While this is an impressive improvement over aspirin, it still must be recalled that 4–14% of patients taking ibuprofen will experience drug-induced gastrointestinal irritation, and three of every 1,000 long-term users will experience ibuprofen-related gastrointestinal bleeding. Researchers have found that 27% of patients who had used ibuprofen on an extended basis had evidence of gastric ulcer formation, even if they had not experienced physical distress from the compound at the time. This risk is increased if the user also ingested alcohol on a regular basis (Virani, Bezchlibnyk-Butler, & Jeffries, 2009).

Naproxen

Naproxen is another propionic acid compound. There is evidence suggesting that naproxen's anti-inflammatory action may be stronger than that of aspirin, and it also has an antipyretic effect, possibly by inhibition of prostaglandin in the hypothalamus region of the brain. But because naproxen only has a limited antiplatelet effect, it is of limited use in the treatment of cardiovascular disease or preventing heart attacks (Hutchison, 2004; Solomon, Glynn, Levin, & Avorn, 2002). When ingested orally, naproxen begins to work within 1 hour, and its analgesic effects last for 7–8 hours. In the circulation, naproxen binds to blood proteins, which can absorb only so many naproxen molecules before they are saturated, and the other molecules float in the circulation without binding to a protein. When prescribed by physicians, it was found that the steady state blood level was achieved when the patient took 500 mg twice a day for 2–3 days (American Society of Health System Pharmacists, 2008). The elimination half-life of naproxen in the healthy adult is 10–20 hours. About 30% of a given dose is biotransformed by the liver into the inactive metabolite 6-desmethylnaproxen, and only 5–10% of a single dose is excreted unchanged.

Complications Caused by OTC Analgesic Use

The OTC analgesics are hardly “safe” medications, and they account for almost a quarter of the adverse drug reactions reported to the Food and Drug Administration (FDA). All of them have significant interactions with other medications. In the section to follow, we will discuss some of the complications and interactions caused by each of the OTC analgesics.

Acetaminophen

There is little known about the phenomenon of cumulative dose toxicity induced by chronic acetaminophen use (Smith, 2007). Acetaminophen does have cumulative effects on the liver, and to avoid this the patient is warned not to use this compound for more than 10 days unless directed to do so by a physician. Acetaminophen has also been implicated as the cause of anaphylactic reactions on rare occasions, although the mechanism by which acetaminophen might trigger such a massive allergic response is not known at this time. It is also *nephrotoxic*, which is to say that its continued use at too high a dosage level might prove to be toxic to the cells of the kidneys. Its use was also once thought to be associated with the development of ESRD,¹⁵ but this possibility has been ruled out (Fored et al., 2001; Rexrode et al., 2001). However, as with all medications, acetaminophen should be used only when the potential benefits outweigh the possible risk associated with its use.

Medication Interactions Involving Acetaminophen

Individuals who use acetaminophen for extended periods of time might find that it interferes with the anticonvulsant effects of lamotrigine, which is a matter of concern for those persons who rely on the latter compound for seizure control (Wilson et al., 2011). It is suggested that the individual consult a physician or pharmacist about the possibility of long-term interaction effects from these two compounds. There is also evidence suggesting that acetaminophen attenuates if not blocks the effects of many selective serotonin reuptake inhibitors (SSRIs) such as citalopram. There is a need for further research into the mechanism(s) by which this occurs, and whether short-term use of acetaminophen is less likely to cause this effect, as opposed to longer-term use (Warner-Schmidt, Vanoverb, Chena, Marshalia, & Greengardia, 2011).

¹⁵End-stage renal disease, briefly discussed earlier in this chapter.

Alcohol is known to interact with acetaminophen, with potentially serious side effects, particularly impacting liver functioning. While this list is not exhaustive, it does reflect the fact that this OTC medication has the potential to interact with prescription medications.

Aspirin

Aspirin is the most commonly used compound in the United States; however, aspirin is hardly safe: Adverse effects of aspirin are usually dependent on the age of the individual and the dose (Half, Fokra, & Arber, 2016). Aspirin-induced hemorrhage is perhaps the most significant adverse reaction. However, users often report other adverse reactions such as anorexia, nausea, and vomiting.

The daily use of aspirin increases the individual's risk for major bleeding, in either the brain or the gastrointestinal tract, by 55% (DeBerardis et al., 2012). Even doses as low as 75 mg a day can significantly increase the user's risk for ulcers and bleeding in the gastrointestinal tract (Iijima, 2016). These gastric ulcers are thought to reflect aspirin's ability to block the normal action of COX-1. Aspirin users who ingest it with acidic compounds such as coffee, fruit juices, or alcohol increase their risk of gastrointestinal irritation, as the irritating effects of each compound enhance those of the other. For these reasons, aspirin is not recommended for patients who have a history of ulcers, bleeding disorder, or other gastrointestinal disorders (Iijima, 2016).

Although aspirin allergy is rare in the general population (0.2%), approximately 20% of those individuals with any kind of an allergy will be allergic to aspirin. These patients are also likely to demonstrate cross-sensitivity to the other NSAIDs (Wilson et al., 2011). Those individuals with the “aspirin triad,” that is to say nasal polyps, asthma, and chronic rhinitis, should not use aspirin or any other NSAID except under a physician's supervision (Wilson et al., 2011). Between 5 and 15% of asthma patients who use aspirin will experience a serious adverse reaction, and if the individual should also have a history of nasal polyps, this could increase to as high as 40%.

One would intuitively expect that aspirin would have little impact on the respiratory system. Unfortunately, this is not true: Approximately 33% of patients who use aspirin for an extended period of time develop a breathing problem(s), which seems to reflect the ability of aspirin to interfere with the normal actions of COX-1. Between 4 and 11% of asthma patients who use aspirin on a regular basis will experience an aspirin-induced bronchial spasm at some point (Barr et al., 2007). Paradoxically, regular use aspirin can have a mild protective effect against the development of asthma in later life. The mechanism for this apparent paradox is not known

at this time. Unfortunately, aspirin (and the other COX inhibitors) can block the development of an immune response following an inoculation against various viral infections, including the influenza inoculation offered each year (Ryan, Malboeuf, Bernard, Rose, & Phipps, 2006). Further research is necessary to support this finding, but it does seem to account for why older individuals, who frequently use COX-2 inhibitors for a variety of problems, do not seem to respond as well to inoculations as do younger patients. It may also account for the observation that aspirin use for symptomatic relief while the patient has a rhinovirus seems to extend the duration of the cold by a small degree.

Patients on anticoagulant therapy involving compounds such as heparin or warfarin should not use aspirin except as directed by a physician. The combined effects of aspirin and the anticoagulant medication might result in significant unintended blood loss if the patient were to have even a minor accident, and might even contribute to a hemorrhagic stroke (He, Whelton, Vu, & Klag, 1998). Long-term aspirin use has also been found to increase the individual's risk of developing macular degeneration, possibly by as much as 200%. Thus, the attending physician must weigh the potential benefits from the use of aspirin against the dangers in these individuals.

The combination of NSAIDs is dangerous, and should not be attempted except under a physician's supervision (Wood, Lanus, & Hennekens, 2016). All NSAIDs can induce **tinnitus**¹⁶ in high doses, or if used simultaneously. A very rare but potentially deadly side effect of aspirin is **hepatotoxicity**, a condition in which the liver begins to fail to filter poisons from the blood. Also, aspirin has been known to induce clinical depression in rare users, and in the elderly it has been known to induce or exacerbate anxiety states. Because of age-related changes in blood flow and liver function, elderly NSAID users are at higher risk for toxic reactions to any of the NSAIDs. These normal age-related changes make it more difficult for the body of an older NSAID user to biotransform and then excrete these compounds, adding to the danger of toxicity from the NSAID being used. Further, because of its ability to interfere with COX-1 in the renal system, aspirin can contribute to both kidney failure and end-stage renal disease (ESRD) in rare cases (Foreed et al., 2001).

In the last quarter of the 20th century, scientists discovered that the use of an NSAID such as aspirin to treat the symptoms of a viral infection was a two-edged sword. While it might provide some symptom relief, aspirin might also contribute to the development of Reye's syndrome in

children who have a viral infection (Jeffreys, 2004; Stimmel, 1997a). Acetaminophen is often suggested as an alternative to aspirin or other NSAIDs if the child should need symptomatic relief.

The anti-inflammatory effect of the NSAIDs, especially aspirin, appears to interfere with the effectiveness of the intrauterine devices (IUDs) used to prevent pregnancy. While aspirin reduces sperm motility by up to 50% when used at therapeutic doses, this is not to suggest that aspirin should be thought of as a form of birth control, nor does the reduced motility outweigh the reduction in IUD effectiveness. However, aspirin use would seem to make it harder for a couple to have a child, should they wish to do so. Finally, it should be noted that an aspirin overdose can result in permanent organ damage, or the death of the individual who ingested the overdose.

Medication Interactions Involving Aspirin¹⁷

The range of potential drug interactions between aspirin and other compounds has not been investigated in detail (Masclee et al., 2014). Individuals who are taking low-dose aspirin for anticoagulant purposes should not use other NSAIDs except under the supervision of a physician because of the increased risk of gastrointestinal bleeding (Masclee et al., 2014). Persons being treated for high levels of uric acid in the body should not use aspirin except as directed. Even at normal dosage levels, aspirin can interfere with the body's ability to excrete uric acid and block the action of the medication probenecid, which is used to treat high blood uric acid levels. Acetaminophen is often suggested as an alternative to aspirin if the patient should require analgesia (Wilson et al., 2017).

Because of its ability to interfere with the normal function of COX-1, aspirin should not be used by patients with hypertension except as directed by a physician. Aspirin-induced COX-1 inhibition interferes with normal kidney function, and may contribute to fluid retention, increasing the work load on the heart (Wilson, Shannon, & Shields, 2015). Also, patients using low-dose aspirin should not take vitamin E, which also has an anticoagulant effect, to minimize the danger of excessive bleeding (Harkness & Bratman, 2003). Further, *any* of the NSAIDs can interfere with the body's ability to metabolize folate, resulting in higher than normal folate levels (Harkness & Bratman, 2003). High

¹⁶See Glossary.

¹⁷It is not possible to list every possible interaction between aspirin and other compounds. A physician or pharmacist should be consulted before the simultaneous use of two or more compounds, even if one is "only" an OTC analgesic.

folate levels pose a health risk for the individual, thus making the concurrent use of these compounds a dangerous practice.

Patients taking the prescription medication valproic acid will experience higher than normal levels of this compound if they are simultaneously using aspirin, because the aspirin molecules will bind at the blood protein binding sites normally utilized by the valproic acid molecules (DeVane & Nemeroff, 2002). The patient should discuss his/her use of this compound, and aspirin use, with the attending physician to minimize the risk of an adverse outcome.

Individuals who plan to consume alcohol should not use aspirin immediately prior to or during the period of active alcohol use. There is strong evidence to suggest that aspirin interferes with the activity of the enzyme gastric alcohol dehydrogenase, which starts to break down alcohol in the stomach before it reaches the circulation. Finally, persons who are using aspirin should not use the herbal medicine ginkgo biloba, because the combination of these two compounds can result in excessive bleeding (Cupp, 1999). There is also evidence suggesting that aspirin attenuates if not blocks the effects of many SSRIs such as citalopram. There is a need for further research into the mechanism(s) by which this occurs, and whether short-term use of acetaminophen is less likely to cause this effect as opposed to longer-term use (Warner-Schmidt et al., 2011). While this list is not exhaustive, it does reflect the fact that this OTC medication has the potential to interact with prescription medications.

Ibuprofen

As an NSAID, ibuprofen shares most of the same complications caused by aspirin use. It also has a number of drug-specific complications, such as blurred vision in a small percentage of users. This condition usually clears up after the person stops taking ibuprofen. Patients who experience any change in their vision should contact their physician immediately. It has also been implicated in the formation of cataracts, and so patients with preexisting cataracts should use ibuprofen only if directed to do so by a physician. Ibuprofen has been identified as the cause of a skin rash in 3–9% of users, and can cause migraine headaches in both men and women. Other identified side effects include (but are not limited to) heartburn, nausea, diarrhea, vomiting, nervousness, hearing loss, congestive heart failure in persons with marginal cardiac function, and, like aspirin, it can elevate blood pressure (Thompson, 2011). Long-term use increases the user's risk of a myocardial infarction. Acetaminophen has been suggested as an alternative to ibuprofen in patients with hypertension, unless directed otherwise by a physician. Patients who suffer from an autoimmune disease such as systemic lupus

erythematosus ("lupus" or SLE) should not use ibuprofen except under a physician's direction. Further, ibuprofen has been identified as a cause of *aseptic meningitis*, especially in patients with SLE (Rodriguez, Olguin, Miralles, & Viladrich, 2006). It is also possible for patients with no identified autoimmune disorder to develop aseptic meningitis after ibuprofen ingestion.

Medication Interactions Involving Ibuprofen

Persons with what is known as a bipolar affective disorder¹⁸ are often prescribed lithium. If a patient taking lithium should also ingest ibuprofen, the blood levels of lithium could increase as much as 25–60%, a matter of some concern in that lithium has only a very narrow therapeutic window (Pies, 2005). Ibuprofen-related lithium toxicity is more pronounced in older patients, but is possible with younger patients who take these two compounds simultaneously. All patients on lithium should discuss their use of ibuprofen, or any OTC analgesic, with their physician to avoid the danger of drug interactions.

Patients receiving the medication methotrexate should not take ibuprofen except under a physician's supervision, since the latter reduces the rate at which methotrexate is excreted by the body. This may contribute to toxic levels of methotrexate building up in the patient's body. Acetaminophen has been suggested as an alternative to the use of NSAIDs by patients on methotrexate. Further, ibuprofen has been found to block the actions of aspirin in controlling blood clot formation, a matter of concern for patients who use aspirin to avoid a heart attack or blood clot formation (Hutchison, 2004). The concurrent use of different NSAIDs should be avoided unless ordered by a physician. There is also evidence suggesting that ibuprofen attenuates if not blocks the effects of many SSRIs such as citalopram. There is a need for further research into the mechanism(s) by which this occurs, and which antidepressants suffer from this interaction effect (Warner-Schmidt et al., 2011).

Naproxen

Much of the information that is available about naproxen and its effects is based on experience with the prescription-strength form of this compound. Naproxen is an NSAID, and like aspirin should not be used in patients who have any of the symptoms discussed in the "aspirin triad" (discussed earlier) except under a physician's supervision. Because it is also a nonselective COX inhibitor, naproxen might interfere

¹⁸Manic-depression" was an earlier term for this disorder.

with the action of COX-1 in the body, resulting in the possible formation of gastric ulcers and gastrointestinal bleeding. Because of its ability to inhibit the function of COX-1, which serves a protective function in the stomach, patients with a history of gastrointestinal bleeding are advised not to use naproxen except as ordered by a physician.

On occasion, male users have experienced naproxen-induced erectile problems, and inhibited ability to ejaculate. As with any medication, the longer the patient uses the medication the more likely s/he is to develop one or more complications induced by the compound. Long-term users of naproxen are at increased risk for a myocardial infarction and should discuss the risks and benefits of using this medication over extended periods of time with their physician. Other known side effects of naproxen include (but are not limited to) drowsiness, dizziness and/or vertigo, depression, diarrhea, heartburn, constipation, abdominal pain, and possible vomiting (Qureshi & Lee-Chiong, 2004). On rare occasions, patients taking naproxen have experienced side effects such as skin rash, headache, insomnia, loss of hearing, and/or tinnitus. All NSAIDs have been implicated as possible causes of ESRD, and there have been rare reports of patients taking naproxen developing aseptic meningitis (Rodriguez et al., 2006). While this list does not identify every possible consequence of naproxen use, it does serve to identify this compound as a potent one, with great potential for danger to the user.

Medication Interactions Involving Naproxen

Individuals taking another NSAID, such as aspirin, should not concurrently take naproxen except under a physician's direct orders, as the negative side effects of one compound can reinforce those of the other. There is also evidence suggesting that naproxen attenuates if not blocks the effects of many SSRIs such as citalopram. There is a need for further research into the mechanism(s) by which this occurs, and whether short-term use of acetaminophen is less likely to cause this effect than longer-term use (Warner-Schmidt et al., 2011).

OTC Overdoses¹⁹

Acetaminophen

When used as directed, acetaminophen has been called “the safest of all analgesics” (Katz, 2000, p. 100). However, acetaminophen does have significant risks associated with its use.

There are more than 100,000 cases of acetaminophen overdose each year in the United States alone (Fontana, 2008; Mowry, Spyker, Brooks, Zimmerman, & Schauben, 2016). It is surprisingly easy to ingest an acetaminophen overdose, as one would only need to ingest 4,000 mg (eight “extra-strength” tablets) at one time, or less if one were drinking or on a “starvation” diet (“Scientists call for stronger warnings for acetaminophen,” 2002). Long-term ingestion of 4,000 mg a day can also be toxic in some cases, even if the medication is taken in divided doses according to instructions (Dave, Miceli, & Modha, 2008).

Unfortunately, 20% of patients who suffer an unintentional acetaminophen overdose will die, usually from acute liver failure (Fontana, 2008). While it might be possible to perform a liver transplant on an emergency basis, liver transplants are difficult, in part because the demand for new livers exceeds the supply. Even if an emergency liver transplant is performed, 30% of these patients die within a year of the procedure (Fontana, 2008; Russo, 2006). A second group of people who are at risk for unintentional acetaminophen overdose are persons who ingest very large doses of vitamin C²⁰ while using acetaminophen (Harkness & Bratman, 2003). High doses vitamin C appear to interfere with acetaminophen biotransformation, possibly to the point where the effects of acetaminophen become toxic. Again, it is imperative for persons taking any herbal medicine or vitamin supplement to consult with a pharmacist or physician about the relative safety of the compounds they are ingesting.

The standard antidote for an acetaminophen overdose is N-acetylcysteine (NAC). However, it must be administered in the first 48 hours following the ingestion of the overdose to be effective, and its full effectiveness is only seen if administered in the first 12 hours following the overdose (Smith, 2007). Since so many patients unknowingly overdose, they are unlikely to seek medical attention during the critical 48-hour period. By the time the cause of their symptoms is identified it is far too late for anything but an emergency liver transplant.

Another group of acetaminophen overdose patients are those who have intentionally ingested an overdose as part of a suicide gesture or suicide attempt. Acetaminophen is involved in the vast majority²¹ of all intentional drug overdoses. Adolescents who ingest an overdose of acetaminophen usually are making a suicide gesture, and since the first objective evidence of acetaminophen toxicity does not develop until 12–24 hours after the overdose is ingested, the

¹⁹Any known or suspected drug overdose should be assessed by a physician immediately.

²⁰A popular vitamin often taken in large doses for its apparent antioxidant effects.

²¹It is also imperative to keep in mind that multiple agents may have been ingested as part of the suicide attempt.

adolescent is often initially assured that s/he did no harm in the suicide gesture. By the time the adolescent is brought in to the hospital, hours or even days after the overdose was ingested, it is far too late for NAC to be administered, since it must be administered *within 12 hours* of the overdose to be fully effective.

Under normal dosage levels, about 4–5% of the acetaminophen is biotransformed into a toxic metabolite known as N-acetyl-p-benzoquinoneimine (Peterson, 1997). Usually this is not a problem as it is rapidly biotransformed into other, safer metabolites by the enzyme glutathione. However, those who use alcohol heavily on a chronic basis, persons who suffer from malnutrition, those who already have liver damage, and those who ingest an acetaminophen overdose rapidly deplete their livers of glutathione, leaving it vulnerable to acetaminophen-induced liver damage. The untreated acetaminophen overdose will progress through four different stages (Dave et al., 2008): Phase 1 begins within 30 minutes to 24 hours, depending on the size of the dose ingested, during which time the individual will experience vague symptoms of distress, including anorexia, nausea and/or vomiting, and **diaphoresis**²² (Dave et al., 2008; Smith, 2007). Phase 2 starts 24–72 hours after the overdose, and is marked by symptoms such as abdominal pain, oliguria, and a swollen, painful liver. Blood tests will demonstrate abnormal liver function, and the kidneys may show signs of dysfunction (Dave et al., 2008; Smith, 2007). In Phase 3, which begins 72–96 hours after the overdose is ingested, the individual will demonstrate nausea, vomiting, jaundice, and overt symptoms of liver failure (Dave et al., 2008; Smith, 2007). Other possible symptoms include hemorrhage, hypoglycemia, renal failure, and hypotensive episodes. It is during this phase that acetaminophen overdoses prove fatal. If the individual survives Phase 3, she or he will begin the final phase, which starts between 2 days and 4 weeks after the overdose.²³ During this phase, the liver begins to repair itself, a process that can last for months, or years, after the overdose (Smith, 2007).

Aspirin

Aspirin is frequently ingested as part of a suicide gesture or attempt. The estimated toxic dose is about 10 grams for an adult, and about 150 mg/kg for children. Symptoms of an aspirin overdose include headache, thirst, dizziness, tinnitus, confusion and/or delirium, hallucinations, diaphoresis, visual problems, and hearing impairment. Other

symptoms include restlessness, excitement, apprehension, tremor, seizures, stupor, coma, hypotension, and possible death (Wilson et al., 2011). Aspirin overdoses are also associated with bleeding problems as a result of its ability to block the capacity of the blood to clot.

Ibuprofen

Symptoms of an ibuprofen overdose include seizures, acute renal failure, abdominal pain, nausea and/or vomiting, drowsiness, and metabolic acidosis. Symptoms that are life-threatening generally do not occur with ingestion of less than 200 mg per kg of weight (Chung & Tat, 2016). There is no specific cure for an overdose of ibuprofen at this time other than general supportive medical care. Like aspirin, another NSAID, ibuprofen overdoses can result in a tendency for the patient to bleed excessively.

Naproxen

The lethal dose of naproxen in humans is not known at this time, partly due to the infrequency of overdose of this substance (Al-Abri, Anderson, Pedram, Colby, & Olson, 2015). The symptoms of a naproxen overdose include (but are not limited to) lethargy, drowsiness, nausea and/or vomiting, epigastric pain, respiratory depression, coma, hypotension and/or hypertension, and convulsions. Like the other NSAIDs, naproxen overdoses can induce a tendency for excessive bleeding (Thompson, 2011). Treatment is supportive, as there is no specific treatment for naproxen overdose; however, all known or suspected naproxen overdoses should be assessed and treated by a physician.

Over-the-Counter Analgesic Use and the *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition)

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) does not directly address the possibility of OTC medication misuse, which is not surprising since these compounds are rarely misused for euphoria. They were included in this text because their potential for harm is so rarely recognized, and individuals misusing substances are especially at risk for harm from these compounds because of interactional effects with the other substances they are misusing.

²²See Glossary.

²³The exact point at which Phase 4 starts is dependent in part on the amount of acetaminophen ingested.

Chapter Summary

Over-the-counter (OTC) medications, especially the OTC analgesics, are often discounted as not being “real” medicine. In reality, they are potent compounds that are quite popular with the general population. More than 77 million pounds of aspirin are manufactured and consumed each year in the United States (IAF, 2017), and aspirin accounts for only about a quarter of the OTC analgesic market. The OTC analgesics are quite effective in the control of mild to moderate levels of pain, and it has been discovered that when added to the narcotic analgesics in certain circumstances, they might actually enhance the analgesic effects of these more potent

compounds as well. Many of the OTC analgesics have been found to control inflammation associated with autoimmune disorders. Some members of the OTC analgesic family of compounds are thought to suppress certain forms of cancer, or lead to their early detection. While aspirin, the oldest OTC analgesic, is more than a century old, researchers are still discovering new applications for this potent medication. In the latter half of the 20th century, acetaminophen and the propionic acid compounds were introduced as alternatives to aspirin and are sold as OTC analgesics. These compounds all share the potential to interact with prescribed medications, alcohol, and possibly with the more popular illicit drugs.

Chemicals and the Neonate¹

The Potential Consequences of Drug

Use During Pregnancy²

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 17.1** Understand the scope of the problem of substance misuse during pregnancy
- 17.2** Identify the concerns with alcohol use during pregnancy
- 17.3** Identify the concerns with various drugs if used during pregnancy

Despite information received by the general public on the adverse effects of substance abuse in pregnancy, there is still significant substance abuse among pregnant women in the U.S.

—Goler, Armstrong, Taillac, and Osejo (2008, pp. 3–4)

Introduction

Substance use during pregnancy, even the use of some prescribed medications, may have dire consequences for both a pregnant woman and her unborn child. The use of many prescription and over-the-counter medications might also disrupt normal fetal growth and development. Unfortunately, recreational drug use is most prevalent in the age cohort most actively involved in reproduction (Bolnick & Rayburn, 2003). Substance use treatment as an integrated component of prenatal care has been found to reduce the number and severity of drug-induced consequences during pregnancy (Armstrong et al., 2008). Unfortunately, health care providers are often hesitant to discuss substance use disorders (SUDs) with pregnant women (Chang et al., 2008). This might explain why, in many cases, pregnancy in a woman with an SUD has had a negative outcome even if she did receive prenatal care (Chang et al., 2008; Goler et al., 2008). In this chapter, the effects of maternal substance use during pregnancy will be explored.

¹It is the author's belief that *all* recreational substance use during pregnancy is a danger to the fetus, and thus to be avoided.

²Technically, the study of how chemical compounds affect neonatal development is the field of *teratogenicity*. A compound that can harm the fetus is called **teratogenic**.

Scope of the Problem

Maternal substance use during pregnancy is a common problem, with nicotine and alcohol use arguably being the two substances most frequently used during this critical phase of fetal development (Jones, Kaltenbach, Chisolm, & Terplan, 2015). To illustrate, consider the study by Behnke, Smith, Committee on Substance Abuse, and Committee on Fetus and Newborn (2013), which found that 16.3% of pregnant women smoked cigarettes and that 10.8% of women consumed alcohol on a regular basis during pregnancy. Pregnant women will sometimes use other compounds as well: An estimated 4.4% of pregnant women will use an illicit drug(s) during their pregnancy, with the rate of illicit drug use being highest in the 15–17 age bracket. It has been estimated that almost 10% of women of childbearing age meet the criteria for admission to a substance use rehabilitation facility, but that 85% of these women did not perceive the need or are never referred to a treatment program (Zilberman, 2009).

Until recently, physicians usually had to rely on maternal self-report to identify babies who were exposed to alcohol or drugs in utero. If **meconium**³ testing was conducted, the results were usually not available for many days, in part because the physician might be forced to wait that time for the meconium to be expelled following birth. However, Montgomery and colleagues (2008) have suggested that the umbilical cord can be tested for fetal exposure to many compounds commonly misused. The authors found that of 498 umbilical cord tissue samples tested, 32% were positive for compounds such as methamphetamine, cocaine, marijuana, and phenylclidine.⁴ The authors suggested that umbilical cord tissue testing might provide a rapid identification of infants who might require special care following prenatal exposure to these compounds. This would also avoid the problem of maternal **dissimulation**.⁵ However, additional research indicated that meconium testing is superior to the cord sample testing, providing more sensitive results (Colby, 2017).

A Period of Special Vulnerability

Compounds that have a negative influence neonatal growth and development are referred to as **teratogenic** chemicals. The range of teratogenic compounds is vast, and includes many prescribed medications, environmental forces,⁶ and

many of the illicit drugs. The effects of the drugs will vary, depending on when during the pregnancy the woman used the compound(s) in question, the compound(s) used, and the frequency, duration, and intensity of that substance use. For example, early in pregnancy nicotine, alcohol, marijuana, opiates, cocaine, and methamphetamine all have teratogenic effects (Behnke et al., 2013).

Women who misuse alcohol or an illicit drug during pregnancy should automatically be classified as having a “high-risk” pregnancy (Finnegan & Kandall, 2008). The first trimester is especially important to subsequent growth and development: Organ differentiation, for example, takes place during the third through eighth week of pregnancy, often before the mother-to-be is even aware that she is pregnant. Many women with substance use disorders do not even attempt to alter their substance use patterns until after their pregnancy has been confirmed (Bolnick & Rayburn, 2003). Maternal alcohol use can induce epigenetic changes in fetal DNA, possibly with lifelong effects (Stelovich, 2011).⁷ Not surprisingly, many women who knowingly continue to misuse alcohol or drugs during pregnancy were raised by parents who also had substance use problems (Gwinnell & Adamec, 2006).

It was long thought that the placenta protected the fetus from foreign chemicals, a belief that has since been refuted (Minnes, Lang, & Singer, 2011). This, plus the limited fetal ability to break down drug molecules, raises the risk of prenatal damage from chemical exposure. For example, only 60% of the blood that the fetus receives from the placenta is processed by the immature fetal liver. The other 40% of the blood (and any toxins in that blood) directly enters the general circulation of the fetus. In addition, compounds that *are* routed to the liver are not always biotransformed at the same rate as would be the case in the mother's body. This can both allow the toxins more time in the body of the fetus and allow the buildup of potentially fatal levels of some compounds in the fetal circulation. Also, the fetal blood-brain barrier is still developing, allowing many compounds easy access to the developing fetal nervous system (Barki, Kravitz, & Berki, 1998). Finally, the circulatory system of the fetus has lower blood protein levels than the adult, providing fewer binding sites for chemicals that are protein-bound, in effect of increasing the concentration of those compounds in the fetal circulation. All of these factors combine to magnify the effects of toxins in the fetus.

In this era of polydrug use, it can be difficult to isolate the effect of one specific compound of the fetus (Chen & Maier,

³See Glossary.

⁴Each of which is discussed in the appropriate chapter of this text.

⁵See Glossary.

⁶Maternal radiation exposure, her stress level during pregnancy, and maternal diet are all excellent examples of environmental forces that might influence prenatal growth.

⁷A body of evidence suggesting that epigenetic changes introduced into the *mother's* body can also be passed on to the fetus, although this lies outside of the scope of this text (Stelovich, 2011).

2011; Mendelson, Mello, Schuckit, & Segal, 2006; Minnes et al., 2011). Additional factors such as the quality of prenatal medical care and maternal malnutrition influence neonatal growth. Following birth, factors such as being raised in an adverse social environment, or poor postnatal caregiving, also influence the baby's growth and development. Maternal preoccupation with drug use, the effects of poverty, the impact of maternal depression on the parent-child relationship, the need to compete with siblings for parental attention, maternal anxiety, the intense needs of the drug-exposed infant for nurturance and care, all can combine to cause a poor developmental outcome in for the infant, child, and adolescent. It is not surprising that researchers have generally found lasting but usually subtle aftereffects of prenatal drug exposure (Malanga, 2009). However, because there are so many variables involved, scientists have for the most part failed to find a specific pattern to warn health care providers that an infant or child was exposed to the drugs of misuse during gestation.⁸

Although technically, postpartum depression is not a known complication of fetal exposure to maternal substance use, there is a relationship between maternal substance use, depression, and attempted suicide following birth. The team of Comtois, Schiff, and Grossman (2008) examined the hospital records of women who gave birth in Washington state between the years 1992 and 2001. The authors of this study found that mothers who misused substances and who developed postpartum depression were six times as likely to attempt suicide in the first year following the child's birth as were those women who did not misuse substances. Given the central role of the mother as the primary caregiver in the first years of the infant's life, it is clear that maternal behavior certainly influences the growth and development of the child.

The discussion that follows must be interpreted as the current understanding of how maternal substance use affects the infant's growth and development. There is still much to learn in this area, and new information is being added to the existing database on a daily basis. In the following sections, we will examine the latest information on the effects of many compounds of misuse on fetal growth and development.

Alcohol

Between 10 and 19% of pregnant women acknowledge alcohol use at some point during pregnancy (Behnke et al., 2013; Sadock, Sadock, & Ruiz, 2015). Unfortunately, (a) alcohol

easily passes across the placenta into the fetal circulation, (b) fetal blood alcohol levels reach the same level as the mother's in a matter of 15 minutes, (c) alcohol is a known teratogenic compound, and (d) the primary metabolite of alcohol, acetaldehyde, is also teratogenic (Fryer et al., 2009; Rose, 1988). So close is the relationship between the effects of maternal alcohol use and its impact on the fetus that if the mother were alcohol-dependent and had been drinking before giving birth, the infant will be at risk for the alcohol withdrawal syndrome starting 3–12 hours after delivery (American Academy of Pediatrics, 1998).

In the early 1973, maternal alcohol use during pregnancy was identified as a major causal agent for birth defects in this country (Sokol, Delaney-Black, & Nordstrom, 2003). The pattern of developmental problems identified in infants born to mothers misusing alcohol was called the fetal alcohol syndrome (FAS), which is now recognized as both the third most common cause of birth defects in developed countries and as the most preventable (Getzfeld, 2006; Glasser, 2002; Krulewicz, 2005; Sadock & Sadock, 2007; Swift, 2005; Thomas, Warren, & Hewitt, 2010). For each alcoholic beverage consumed per day, the risk for damage to the developing fetus increases (Feldman et al., 2012). Prenatal exposure to alcohol does not automatically cause the *fetal alcohol syndrome* (FAS): Many children who were exposed to alcohol in utero will have some, but not all, of the symptoms of FAS (Cunniff, 2003; Rourke & Grant, 2009). These children were said to have *fetal alcohol effects* (FAE). Although the terms FAS and FAE are still used in the clinical literature, physicians are increasingly using the term *fetal alcohol spectrum disorder* (FASD) for such children (Sokol et al., 2003). However, it is important to point out that FASD is not a recognized diagnostic category, and it remains a theoretical construct (Brown, 2006; Coles, 2011).

Scope of the Problem

Maternal self-report is a notoriously unreliable source of data about alcohol use during pregnancy: Many women do not report the frequency or amount of their alcohol use during pregnancy, while others are left to having to rely on their memory to determine their level of alcohol use during the previous nine months (Chang, 2006; Coles, 2011). Unfortunately, there is no reliable biomarker available to physicians or researchers to help them identify infants exposed to alcohol prior to birth (Bailey & Sokol, 2011). To complicate matters, there are many confounding variables that influence the impact of maternal alcohol use during pregnancy: The stage of fetal development when the alcohol use occurred, the amount of alcohol consumed, the age of the woman, her stress level, diet, concurrent use of illicit drugs or use of

⁸Some might argue that fetal alcohol syndrome, discussed later in this chapter, is an exception to this rule. However, how many infants are exposed to alcohol in gestation who do not develop this condition because they lack the genetic heritage necessary to produce FAS? The answer to this question is not known.

prescribed medications, and cigarette smoking all complicate the problem of early identification of children with FAS or FASD (Bailey & Sokol, 2011). The problem of maternal cigarette smoking is hardly insignificant: 55% of pregnant women who drink are cigarette smokers, and cigarette smoking has itself been identified as a negative influence on fetal growth and development.

*There is no safe level of alcohol use during pregnancy.*⁹ The possibility that the infant will develop FASD is dependent, in part, upon the level of maternal alcohol intake. Consumption of just 4–6 drinks per day will result in two-thirds of the children developing FASD. In spite of awareness of this fact, a telephone survey conducted by Denny and colleagues (2012) found that 7.6% of the pregnant women surveyed had consumed at least one drink in the previous 30 days, and 1.4% had engaged in binge drinking in that time. In contrast to this were the conclusions of Kelly and colleagues (2013). The authors suggested that the consumption of up to two standard units of alcohol *per week* did not appear to have a negative effect on fetal growth and development. However, further research is necessary to confirm these findings, and until confirmed it would appear best for the pregnant woman to abstain from alcohol use.

Consequences of Maternal Alcohol Use

The fetal brain is vulnerable to alcohol exposure, especially in the first trimester. There are multiple mechanisms by which maternal alcohol use can disrupt normal fetal development during this critical phase (Fryer et al., 2009). One mechanism is that the use of alcohol inhibits the production (biosynthesis) of a family of compounds known as *gangliosides* in the developing fetal brain. These enzymes are most active during the first trimester of pregnancy, playing a role in fetal brain development. By blocking the biosynthesis of the gangliosides during the first trimester, maternal alcohol use can prove especially destructive to the growing fetal central nervous system (CNS).

To test the impact of maternal alcohol use on fetal neurological development, Humphriss, Hall, May, Zuccolo, and Macleod (2013) examined the abilities of almost 7,000 children in England who had been exposed to zero up to moderate levels of alcohol during pregnancy. The authors defined “moderate” alcohol use as no more than seven standard drinks in a week’s time; they found that at the age of

10 years, the children who were exposed to alcohol in utero demonstrated a deficit in ability to maintain their balance, an indirect measure of possible neurological damage. The authors concluded that these results reflected chance variation in participant selection or their lack of participants who engaged in high levels of alcohol consumption while pregnant. The authors of the study emphasized that the results did not indicate that maternal alcohol use during pregnancy was harmless.

It has been accepted by researchers that maternal alcohol use during pregnancy can increase oxidative stress and inhibit neural adhesion within the developing brain of the fetus. Further, the period of prenatal development is a high-risk period for alteration of gene expression (epigenesis) by an environmental factor such as alcohol, leading to long-term (if not lifelong) changes in gene expression for the infant. This might be one reason why different structural components of the developing brain are especially vulnerable to alcohol’s effects at different points in gestation (Thomas et al., 2010). Radiographic studies of the brains of infants born to mothers misusing alcohol have found structural damage to the corpus callosum, if not the absence of this vital brain structure (known as **agenesis**¹⁰ of the corpus callosum). Damage to such structures in the brain often results in the development of seizure disorders and might account for the findings of Bell and colleagues (2010), who found a significantly higher incidence of seizure disorders in children exposed to alcohol in utero.

As scientists learn more about FAS, it has been discovered that 17% of infants with FAS are either stillborn or die shortly after birth (Bailey & Sokol, 2011; Fryer et al., 2009; Renner, 2004a). The annual cost to society for providing remedial services to children with FAS or related disorders in the United States is estimated to be approximately \$700 million a year (Bhuvaneswar & Chang, 2009).

Children with FAS will have a characteristic pattern of facial abnormalities, one in five infants with FASD will have a major birth defect, and approximately half will have an IQ that falls below 70¹¹ (Coles, 2011). A large percentage of the remaining children will have an IQ in the borderline range of intellectual function, placing them at risk for academic, vocational, and social adaptation problems later in life. Infants who are born with severe FAS usually have a lower-than-normal birth weight and **microcephaly**¹² at birth. Noninvasive neurodiagnostic imaging studies of the brains of children exposed to alcohol in utero often reveal damage to the cortex,

⁹Some women, having been told that they should ingest *no more* than one standard drink in 24 hours, believe that they can “save up” each day’s acceptable level of alcohol intake, so that they can go on a binge later. Unfortunately, research has found that even one such binge will place the fetus at risk for FAS/FASD and other developmental problems (Brown, 2006).

¹⁰See Glossary.

¹¹An IQ of 70 or below is often used as the criterion for determination of eligibility for special education or social support services.

¹²See Glossary.

cerebellum, basal ganglia, hippocampus, caudate nucleus, and corpus callosum of their brains (Carter et al., 2012; Cunniff, 2003; Fryer et al., 2009). These findings are important because the **corpus callosum** is the region of the brain that transfers information from one hemisphere to the other, while the caudate nucleus and the cerebellum are involved in the coordination of muscle movements.

In later life, these children may experience behavioral problems such as attention deficit hyperactivity disorders (ADHD) (Greenbaum et al., 2009; Peters, 2007), as well as weaker emotional processing and social cognition skills than normal children. While behaviorally children with FASD appear similar to children with ADHD, it has been hypothesized that there are different neurological mechanisms between the two disorders (Greenbaum et al., 2009). The authors suggested that their behavior might reflect damage to the orbitofrontal region of the brain rather than those regions of the brain traditionally thought to be involved in ADHD. Children with FASD also experience short attention span; anger control issues; impulsiveness;¹³ self-abusive behaviors; poor coordination; cardiac, renal, and visual system disturbances; learning disabilities; and a variety of other developmental delays (Bhuvanewar & Chang, 2009; Grinnell & Adamec, 2006; Peters, 2007). It is important to remember that the intensity and number of symptoms that a child with FASD will demonstrate depends on a number of factors, including maternal tobacco use, which is itself a confounding factor as we struggle to better understand FASD.

The low birth weight characteristic of children with FAS appears to at least partially resolve itself by adolescence, and children with FASD usually fall within the normal height and weight range for adolescents and adults their age (Peters, 2007). This does not negate the fact that these children often need lifelong social service support(s). There is also strong evidence that children exposed to alcohol in utero are at increased risk for developing an alcohol use disorder of their own later in life¹⁴ (Gilman, Bjork, & Hommer, 2007; Jones et al., 2015).

Other Consequences of Maternal Alcohol Use

There is also a mounting body of evidence suggesting that maternal alcohol use during pregnancy will increase the

child's risk of developing acute lymphoid leukemia later in life (Menegaux et al., 2006). Gauthier (2015) reported that pregnant women who are heavy drinkers have a 35-fold greater chance of premature birth than a nondrinking woman the same age. Further, infants who were exposed to alcohol in utero are at increased risk for anemia at birth as well as the poorly understood sudden infant death syndrome (SIDS) (Bailey & Sokol, 2011; Carter et al., 2012). Finally, there is evidence that maternal alcohol use during pregnancy increases the chances that the child will themselves grow up to have an alcohol use disorder (Alati et al., 2006). It should be noted that all of these problems might develop in the infant exposed to alcohol in utero even if she or he does not develop a clinical fetal alcohol spectrum disorder.

Breast Feeding and Alcohol Use

Mennella and Pepino (2010) found that women who have a familial history of alcoholism have a blunted response to prolactin if choosing to breast-feed. Such women tend to produce less breast milk and produce it for a shorter period of time per feeding episode. In such women, the authors observed a tendency for the women to breast-feed the baby more frequently, but found little evidence to support the myth that alcohol use during breast feeding enhances milk production.

Alcohol in the mother's circulatory system passes freely into her breast milk and will quickly reach 90–95% of the level of alcohol found in her general circulation (Virani, Bezchlibnyk-Butler, & Jeffries, 2009). Fortunately, even if the infant were to feed while the mother was quite intoxicated, the amount of alcohol ingested by the infant along with the mother's milk would be diluted throughout the baby's system, resulting in a lower blood alcohol level for the infant than the mother's (Heil & Subramanian, 1998). However, even this limited alcohol exposure is associated with abnormal gross motor development in the infant, with a dose-dependent relationship between the mother's alcohol use and infant psychomotor problems. Further, maternal alcohol use can cause an abnormal development of the neonate's immune system, possibly lasting for the rest of the child's life (Gauthier, 2015). It is also theoretically possible that maternal alcohol use during the period when she is breast-feeding might interfere with the development of the infant's immune system, again possibly with lifelong consequences. For these reasons, maternal alcohol use during pregnancy and the time when she is breast-feeding is not suggested (Sadock et al., 2015).

Disulfiram Use During Pregnancy

Disulfiram is often used as an adjunct to the treatment of alcohol addiction. It has been discovered that during gestation

¹³ Making them vulnerable to legal problems when the individual impulsively breaks the law.

¹⁴ Raising an interesting question: Is the child's later increased risk for an alcohol use disorder caused by the exposure to alcohol in utero, their genetic heritage, environmental forces, or an interactional effect among all three forces?

a metabolite of disulfiram, diethyldithiocarbamate, can bind to lead, and might bring that lead across the placental barrier. Fetal exposure to lead is known to disrupt normal neurological growth and development in the fetus, and so the use of disulfiram during pregnancy is not recommended.

Use of Amphetamines and Amphetamine-Like Compounds During Pregnancy

In spite of the media emphasis on the methamphetamine “epidemic” in this country, there is surprisingly little research into the specific effects of maternal amphetamine use on fetal growth and development (Finnegan & Kandall, 2005; Jones et al., 2015; Minnes et al., 2011). It is known that, unlike babies born to mothers who are actively drinking or using opioids, babies born to a mother who is using an amphetamine compound do not seem to be born “addicted” to the amphetamine¹⁵ (Erickson, 2007).

There is evidence that women who use methamphetamine during pregnancy are more likely to be younger, live alone, have a lower income and a lower educational level, and receive less prenatal care than their non-abusing counterparts (Winslow, Voorhees, & Pehl, 2007). Once they learn they are pregnant, the majority of women attempt to decrease their frequency and level of methamphetamine abuse or stop it entirely (Terplan, Smith, Kozloski, & Pollack, 2009). They remain reluctant to seek prenatal care because of their fear of legal sanctions or the stigma associated with methamphetamine use.

Preliminary evidence suggests that infants exposed to amphetamine compounds in utero are more likely to experience abruptio placentae (premature birth), suffer from congenital brain lesions, and have a visual cortex dysfunction (Brust, 2004; Cloak, Ernst, Fujii, Hedemark, & Chang, 2009; Lehne, 2013; Rawson & Ling, 2008). Infants born to mothers using methamphetamine are 3.5 times as likely as to be small for their gestational age compared to other infants (Minnes et al., 2011; Wright, Schuetter, Tellei, & Sauvage, 2015), which is an indirect measure of neurological growth and maturity in the baby at birth. Infants exposed to methamphetamine in utero are significantly more likely to demonstrate higher levels of emotional reactivity at ages 3 and 5, as well as higher levels of anxiety and depression, than infants

who were not exposed to this compound in utero (LaGasse et al., 2012).

There is also evidence that infants exposed to methamphetamine in utero have altered neurological function in the frontal stratal and limbic regions of the brain¹⁶ (Sowell et al., 2010). The infant’s risk of neurological harm appears to be dose-related, with those infants with a greater degree of exposure having the highest degree of risk for neurological damage (Erickson, 2007). However, further research is needed to confirm these initial findings. Indirect evidence suggests long-term (possibly lifelong) changes in DNA expression for the mother and the infant, leaving the infant vulnerable to diabetes or cancer later in life (“Hunger leaves its mark on fetal DNA,” 2008). Animal research would also suggest that prenatal exposure to methamphetamine might predispose the infant to the neurotoxic effects of this compound later in life (Heller, Bubula, Lew, Heller, & Won, 2001). It is not known whether this occurs in humans at this time, but it is suggestive of a vulnerability to methamphetamine neurotoxicity later in life. Again, further research is necessary both to confirm these theories and to trace the implications of these findings across the life span for both the mother and the infant.

There is a strong body of evidence suggesting that maternal use of methamphetamine is associated with such problems as anemia, premature birth, and a tendency for the placenta to separate from the wall of the uterus (Winslow et al., 2007). Other possible consequences of maternal methamphetamine use might include meconium aspiration, infection of the amniotic cavity, placental hemorrhage, and neonatal anemia. Following birth, there is evidence suggesting that the infant is vulnerable to psychosocial developmental problems and frontal lobe dysfunction, as well as sleep abnormalities and birth defects such as a cleft lip (Brust, 2004). It is not known what percentage of methamphetamine-exposed infants will experience these or other problems, and Erickson (2007) suggested that the majority of infants exposed to methamphetamine in utero will reach most normal developmental milestones on time.

The amphetamines induce a state of anorexia in the user, and maternal malnutrition potentially contributes to epigenetic changes for the infant. These epigenetic changes appear to leave the infant vulnerable to diabetes or cancer later in life (“Hunger leaves its mark on fetal DNA,” 2008), and might leave the individual more vulnerable to the neurotoxic effects of alcohol later in life. Further research is necessary to confirm and explore the implications of these

¹⁵However, because of the problem of polydrug abuse, it is still possible for the infant to be addicted to another compound(s) that the mother was using.

¹⁶Regions where methamphetamine is known to have a neurotoxic effect in adults.

findings, which contradict research suggesting a low potential for long-term damage to the fetus if it (a) receives proper post-delivery medical care, (b) receives adequate parenting, and (c) is allowed appropriate social interactions with other children¹⁷ (Erickson, 2007). While it appears evident that amphetamine use does result in damage to the fetal brain, the issue of whether there are methamphetamine-specific consequences to the fetus remains unclear at this time.

Amphetamine Use and Breast-Feeding

The problem of maternal amphetamine use during breast-feeding needs further research, but it is known that the concentration in breast milk may be up to eight times that in the mother's blood (Jones et al., 2015). It is known that some amphetamine ingested by the mother will be found in the breast milk, and that it can induce neonatal irritability and poor sleep (Virani et al., 2009).

Barbiturate and Barbiturate-Like Drug Use During Pregnancy

Fortunately, compounds such as the barbiturates and barbiturate-like medications are only rarely prescribed, and their misuse is quite uncommon. All of these compounds cross the placenta into the fetal circulation (Mihic & Harris, 2011). If misused in high doses by the mother for a sufficient period of time, following birth the infant will experience a neonatal withdrawal syndrome similar to that induced by alcohol. This infant neonatal withdrawal syndrome might require up to 4 days to develop after birth, depending on the exact compound(s) being misused and the total dose ingested by the mother. If the physician is unaware of the mother's substance use disorder, the neonatal withdrawal syndrome could be mistaken for hypoglycemia, sepsis, a range of cardiovascular disorders, or meningitis. Physicians have found that phenobarbital, a barbiturate with a long therapeutic half-life, will allow for the gradual withdrawal from these compounds for the infant. Since these compounds are so rarely prescribed, and even less likely to be misused in today's world, they will not be discussed further in this chapter.

Benzodiazepine Use During Pregnancy

Research has shown that small amounts of benzodiazepine ingested by the mother will cross the placenta and enter

the fetal circulation, although the exact amount varies from compound to compound. For example, fetal blood levels of diazepam will reach 10% of the maternal blood level, while lorazepam only reaches 7% (Virani et al., 2009). There are numerous anecdotal case reports suggesting that benzodiazepine use during pregnancy can result in facial abnormalities such as cleft palate, congenital heart defects, hernias, and pyloric stenosis. However, the research has failed to support the theory that benzodiazepine use is the cause of these problems (Iqbal, Sobhan, & Ryals, 2002), and the teratogenic potential of benzodiazepines remains unclear at this time. It is recommended that when used during pregnancy, the prescribing physician should use the lowest possible dose for the shortest time necessary (Iqbal et al., 2002; Raj & Sheehan, 2004). As with any medication, they should be used only when the potential benefits are thought to outweigh the possible risks of their use, in the opinion of the attending physician.

Maternal benzodiazepine addiction will, following birth, force the infant to go through benzodiazepine withdrawal (Hudak, Tan, Committee on Drugs, & Committee on Fetus and Newborn, 2012). This withdrawal process is potentially life-threatening for the infant, and the attending physician should be made aware of the mother's dependence on benzodiazepines to enable him or her to prescribe appropriate medications to avoid or control the poorly understood benzodiazepine neonatal withdrawal process.

Benzodiazepine Use During Breast-Feeding

The known benzodiazepines will cross over from the maternal circulation into breast milk. However, the amount that crosses over into the infant's circulation is so small that these compounds were deemed safe for the nursing mother to use (Ciraulo & Knapp, 2009). However, maternal diazepam use has been identified as a possible cause of neonatal sedation and lethargy (Iqbal et al., 2002). The benzodiazepines are biotransformed in the liver, an organ that is not fully developed in the neonate, and so the prescribing physician must weigh the potential benefits of the benzodiazepine to the mother against the risks to the nursing infant.

Bupirone Use During Pregnancy

It is not recommended that the expectant mother use bupirone unless a physician determines that the anticipated benefits outweigh the potential risks to the fetus. Animal research has suggested that there is an increased risk of stillbirth, but there is little evidence of long-term cognitive deficits in rats exposed to bupirone in utero.

¹⁷Unfortunately, if the mother continues to use methamphetamine, her ability to provide these things would be compromised, leaving the child to suffer.

Cigarette Smoking During Pregnancy

Each year in the United States approximately 4 million women give birth. Of this number, between 16.3% (Behnke et al., 2013) and 28.6% (Chang, 2010) smoked cigarettes while pregnant. Approximately 50% of women who become pregnant stop smoking, at least during their pregnancy (Hall, 2014). This is fortunate, since many of the compounds found in cigarette smoke are able to cross the placenta into the fetal circulation (Buka, Shenassa, & Niaura, 2003). Some of the consequences of maternal smoking during pregnancy include low birth weight, premature rupture of the membranes, premature labor, abruptio placentae, myocardial infarction,¹⁸ venal and arterial thrombosis, vitamin and mineral absorption problems, placenta previa, and sudden infant death syndrome (SIDS) (Bhuvanewar & Chang, 2009; Brust, 2004; Burns, 2008; Chang, 2010; Minnes et al., 2011). Maternal cigarette use is thought to account for 20% of low birth weight children, 8% of cases of premature labor, and 5% of the cases of perinatal death each year in the United States. The causal mechanism for premature labor and for underweight infants is thought to be nicotine-induced constriction of the blood vessels in the placenta, reducing the flow of blood to the fetus. Emerging evidence does suggest that if the woman stops smoking in the early stages of pregnancy, the fetus will be less likely to be underweight at birth (McGowan et al., 2009).

There is a possible relationship between maternal cigarette smoking and the failure of the limbs to develop properly (*congenital limb deficiency*). There is also evidence suggesting that infants born to mothers who smoke have reduced lung capacity, although the causal mechanism for this is not known. Weitzman, Govil, Liu, and Lalwani (2013) uncovered evidence that adolescents whose mothers smoked during pregnancy were nearly three times as likely to experience a low-frequency unilateral hearing loss during adolescence. Maternal smoking during pregnancy can induce epigenetic changes in ten different genes in the genome of the fetus, including some involved in the metabolism of tobacco products (Joubert et al., 2012). These epigenetic changes might account for the increased risk for the development of schizophrenia in early adulthood in infants whose mothers were heavy smokers during gestation.

There is a counterintuitive relationship between maternal smoking during pregnancy and the child's weight during adolescence: Adolescents whose mothers smoked during

pregnancy have a greater risk of obesity (Haghigi et al., 2012). The authors speculate that this might reflect subtle changes in the reward system in the fetus that are not expressed until adolescence, but this weight condition might also reflect the epigenetic changes initiated by the mother's smoking before birth. There has been some controversy about whether maternal cigarette smoking during pregnancy might be associated with behavioral problems (especially substance use, such as cigarette smoking) during the child's adolescence (Buka, Shenassa, & Niaura, 2003; Guilbert & Krawiec, 2003; Keyes, Legrand, Iacono, & McGue, 2008; Minnes et al., 2011). However, it is not clear whether maternal cigarette smoking is a causal agent in the development of these problems or just a confounding variable.

To explore this possibility, D'Onofrio and colleagues (2012) examined data from two large cohort studies, one in Sweden and the other in the United States, and concluded that the apparent association between maternal cigarette smoking and subsequent adolescent substance use problems were due to shared familial factors. In contrast, Gaysina and colleagues (2013) found that children whose mothers reported having smoked during pregnancy were more likely to have conduct problems than children born of nonsmoking mothers. This was true even if the child was raised by an adopted parent. The authors also found a correlation between the number of cigarettes smoked per day by the mother and the probability that the child would develop a conduct disorder later in life. This would suggest that maternal cigarette smoking was indeed related to later behavioral problems in the child or adolescent. Additionally, there have been numerous studies linking in utero tobacco exposure to childhood cancers, as well as greater risk for a variety of diseases in adulthood, including lung disease, heart disease, and diabetes (Jones et al., 2015).

Prenatal Exposure to Environmental Tobacco Smoke

Women who are exposed to secondhand smoke while pregnant are at risk for vaginal bleeding (Centers for Disease Control, 2004). Further, maternal cigarette use appears to increase the odds that the infant will develop asthma and a conduct disorder in later life. Fetal exposure to secondhand tobacco smoke was associated with an increased incidence of hearing loss later in life, although the mechanism by which exposure to environmental tobacco smoke is able to cause this outcome is not known at this time (Weitzman et al., 2013).

An often-overlooked venue for infant exposure to cigarette smoke is parental smoking in the motor vehicle (Nabi-Burza et al., 2012). The authors found that less

¹⁸Admittedly a rare complication of pregnancy, being seen in only 1 in every 35,000 pregnancies.

than one-third of parents who smoked had a “no smoking in the car” policy that they enforced both upon themselves and upon passengers in the motor vehicle. Exposure to cigarette smoke in a small, confined space such as a motor vehicle exposes the infant or child to significant levels of smoking-produced microscopic particles that remain in the air even if a window is open, according to the authors, who pointed out that exposure to these microscopic pollutants increases the infant or child’s possibility of developing a respiratory tract infection, SIDS, ear infections, or asthma.

Maternal Use of “E-Cigarettes” (Electronic Cigarettes)

Nicotine is one of the most lethal poisons obtained from plants, and is a component of e-cigarettes. Unfortunately, there has been virtually no research into the effects of maternal e-cigarette use during pregnancy. Thus far, it appears that studies investigating e-cigarettes omit pregnant women as participants (Bryce & Robson, 2015). Studies thus far on perceptions of the impact of e-cigarettes on the developing fetus do show that they are viewed as less harmful than traditional cigarettes (Wigginton, Gartner, & Rowlands, 2017), although research is certainly needed to confirm or refute this assumption.

Smoking and Breast-Feeding

It is recommended that the mother abstains from tobacco if she plans to breast-feed her infant. Nicotine tends to be concentrated in breast milk (potentially up to three times that in the mother’s bloodstream; Jones et al., 2015), and it has a half-life in breast milk of about 1.5 hours. The total nicotine concentration in breast milk depends on the number of cigarettes the mother smokes and the time between her last cigarette and the time that she breast-feeds the infant. Since nicotine is a stimulant, and stimulants tend to have an anorexic side effect, it is not surprising to learn that infants born to smoking mothers and who breast-feed tend to gain weight more slowly than other infants.

Nicotine Replacement Therapy (NRT) During Pregnancy

Intuitively, one might expect that nicotine replacement therapy for a pregnant woman would be contraindicated. However, some do see NRT as more helpful to the fetus than if the mother were to continue smoking, since there are over 4,000 known compounds in cigarette smoke, many of which hold the potential to interfere with normal fetal growth and

development. The nicotine replacement therapy will thus reduce fetal exposure to chemicals from over 4,000 to just one, and thus the benefits outweigh the potential hazards to the fetus. Some countries indicate that intermittent-dosage NRT (such as nicotine gum) can be used, whereas other countries (such as the United States) indicate that no NRT should be used during pregnancy (Verbiest et al., 2017).

Bupropion Use During Pregnancy

Bupropion is often used as an aid in smoking cessation. Its safety during pregnancy has not been established, and the effects of this compound on fetal growth and development have not been studied in detail. What is known is that the substance and its metabolites do end up in the fetus, crossing the placenta (Fokina et al., 2017), but seemingly at levels that may not necessarily impact the infant (Jones et al., 2015).

Cocaine Use During Pregnancy

During the peak of the last wave of cocaine use in the United States, it was estimated that 100,000 infants who were exposed to cocaine in utero were born each year (Minnes et al., 2011). The implications of such maternal cocaine use on fetal growth and development remain unclear, as there is no cocaine-specific pattern of symptoms or organ damage that might identify the child exposed to cocaine in utero. During the peak years of the last wave of cocaine use in this country, newspapers made dire predictions of an epidemic of “crack” babies about to descend on society. These children would bring with them a need for huge expenditures for special education and social service support, according to the media (Malanga, 2009). Although an estimated 2 million people in this country were exposed to cocaine prior to birth (Minnes et al., 2011), there is little evidence that such an epidemic ever developed.

This is not to say that maternal cocaine use during pregnancy is safe. There is quite a large body of research to date, but the findings have often been inconsistent and questionable, due to methodological weaknesses of the studies (Jones et al., 2015). At present, we do know that exposure to cocaine in utero does result in a negative impact on brain development as well as long-term challenges in regulation of arousal, minimally through the adolescent years (Li, Coles, Lynch, Luo, & Hu, 2016). However, some scientists now believe that the effects of prenatal exposure to cocaine are less than that of maternal cigarette use or of maternal drinking (Lehne, 2013). Because of the developmental immaturity of the infant’s body, the cocaine that is absorbed will

remain in the neonate's blood for days after birth because the infant lacks the ability to rapidly biotransform cocaine (Karch, 2009). Exposure in utero to cocaine shows some evidence indicating that fetal growth may be impacted and that there can be premature placental separation (Jones et al., 2015). Lower birth weight, length, and head circumference have been shown in some studies, although other studies do not show the same findings (Jones et al., 2015). The research does suggest that the infant will experience "lasting, albeit subtle, effects of prenatal drug exposure on brain structure" (Malanga, 2009, p. 2062).

In the 1980s, many states enacted laws to protect the fetus, mandating incarceration for the expectant mother who used cocaine (or other illicit drugs). Such laws had an unintended effect: Many pregnant women who were using cocaine stopped seeking prenatal health care to avoid the danger of prosecution. Other women feared the stigma associated with prenatal cocaine use, and did not admit to the use of cocaine when asked (Zilberman, 2009). Another unintended consequence of such protect-the-fetus laws is that the first medical care that many of these women received during pregnancy was when they arrived at the hospital in labor. This lack of prenatal medical care contributes to the problem, with negative impacts on both the mother and the developing fetus (Coyer, 2017; Hui, Angelotta, & Fisher, 2017).

Cocaine and Breast-Feeding

The data on the effects of maternal cocaine use on the breast-feeding infant is very limited (Zilberman, 2009), but it is understood that the cocaine in the breast milk can potentially have neurological and developmental impacts on the infant (Jones et al., 2015; Sherman, 2015). The cocaine molecule is highly lipid-soluble, and it may be stored in breast milk and then passed on to the infant by the mother during breast-feeding. The cocaine concentration might be *eight times* as high in breast milk as it is in the mother's blood, and for this reason maternal cocaine use during the period when she is breast-feeding is to be discouraged.

Hallucinogen Use During Pregnancy

There is only limited research into the effects of maternal hallucinogen use on fetal growth and development, partly due to the broad spectrum of hallucinogens (Jones et al., 2015). What will follow is a brief description of the effects of the most commonly used hallucinogens on the fetus. It is important to keep in mind that other hallucinogens might also be used, and it is impossible to list every possible hallucinogen and every possible effect of each on fetal growth

and development. However, because so little is known about the pharmacokinetics of the hallucinogens, the use of these compounds by the pregnant or breast-feeding mother is *not* recommended.

LSD Use During Pregnancy

Virtually nothing is known about the effects of LSD use on fetal growth and development. It is, however, not recommended that nursing mothers use this compound, if only because its effects remain unknown.

MDMA Use During Pregnancy

Preliminary research into the effects of MDMA on the fetus would suggest that motor skills and coordination are impacted when measured at 4 months and at 12 months (depending on the amount of MDMA used), in addition to impacts on cognitive development as measured at 12 months, but evidence does not currently support a relationship between use during pregnancy and impact on birth measurements or shortened pregnancy (Jones et al., 2015). The mechanism by which MDMA might cause or contribute to congenital birth defects is not known at this time.

PCP Use During Pregnancy

At most, there is limited information on the effects of phenylcyclidine on the fetus. The available evidence would suggest that infants exposed to PCP in utero are at increased risk for conditions such as hydrocephalus, sleep respiratory problems, and abnormal development of body organs such as the heart, lungs, urinary system, or musculoskeletal system (Brust, 2004). Immediately following birth, infants born to PCP-abusing mothers demonstrate abrupt changes in their level of consciousness, fine motor tremors, sweating, and irritability. There is a possibility that some or all of these effects are caused by polydrug use rather than the use of PCP alone.

Salvia Divinorum Use During Pregnancy

Only recently have studies begun to explore the pharmacokinetics of this compound, and its use prior to or during pregnancy is *not* recommended.

Inhalant Misuse During Pregnancy

Each year in the United States, 12,000 pregnant women are thought to misuse an inhalant at least once (Brust, 2004). The limited literature to date does indicate negative impacts

on the developing fetus, considering both recreational and occupational inhalants (Jones et al., 2015). Current evidence does suggest that inhalant use is a cause of growth retardation in utero, developmental abnormalities, fetal death, neurodevelopmental problems, tremor, and ataxia following birth, as well as lower birth weight and increased risk of SIDS (Sharp & Rosenberg, 2005; Virani et al., 2009). The effects of toluene, which is known to cross the placenta, are still under investigation. However, the liver of the fetus and newborn is still quite immature and unable to metabolize toluene. There is preliminary evidence to suggest that toluene exposure during pregnancy can cause a syndrome similar to the fetal alcohol spectrum disorder (discussed earlier in this chapter), called fetal solvent syndrome (Jones et al., 2015). Bowen, Batis, Mohammadi, and Hannigan (2005) exposed pregnant rats to toluene fumes and found that the pups suffered from growth restriction, as well as a range of physical abnormalities. Toluene and other inhalant exposure by pregnant women should be avoided. Additionally, evidence indicates that the level of inhalants present in breast milk is higher than in the mother's blood, and thus breast-feeding and inhalant use also has significant potential to harm the infant (Jones et al., 2015).

Marijuana Use During Pregnancy

There is only limited research data on the effects of maternal marijuana use on fetal growth and development (Bhuvaneswar & Chang, 2009; Finnegan & Kandall, 2004; Jones et al., 2015). Further, in some research on marijuana use by those who are pregnant, the overlap with tobacco use by participants makes it difficult to isolate the effects of marijuana alone on neonatal growth (El-Marroun et al., 2016). It is thought that the placenta is able to provide the fetus with some degree of protection against marijuana, resulting in fetal THC that only reaches one-sixth that of the mother (Nelson, 2000). Regrettably, even these low levels of THC potentially can have dire consequences on the neurological development of the fetus, as evidenced by MRI studies of cortical thickness of children exposed to cannabis in utero (El-Marroun et al., 2016).

There is evidence based on animal research that the endocannabinoid anandamide helps to guide both the specification of what are known as pyramidal cells and the pattern of axon growth in neurons as cortical neural networks are established (Mulder et al., 2008). Marijuana use during pregnancy holds the potential to interfere with the normal endocannabinoid function in the fetal brain, possibly causing long-term (if not permanent) changes in the brain's physical structure (Gold & Dupont, 2008). This might be the

mechanism through which the subtle neuropsychological deficits reported by Zilberman (2009) develop.

Admittedly, it is difficult to isolate the effects of maternal marijuana use from the effects of tobacco or other drugs. Still, preliminary evidence suggests that maternal marijuana use during pregnancy or while breast-feeding may be linked with low birth weight, premature birth, and behavioral problems in childhood (Jones et al., 2015). These findings are complicated by the fact that women who smoke marijuana during pregnancy often are also cigarette smokers, and these are known side effects of cigarette smoking during pregnancy. Other potential **confounding variables**¹⁹ that must be considered include (a) the potency of the marijuana being smoked, (b) the frequency of maternal marijuana use, (c) how deeply the mother inhaled when she did smoke marijuana, and (d) what other compounds (pesticides, for example) were intermixed with the marijuana smoked. Finally, although it is assumed that THC is the only compound that will impact fetal growth and development, marijuana smoke contains a number of different compounds, and their impact on fetal growth and development has not been studied.

In spite of these unknown variables, scientists have tentatively concluded that children whose mothers use marijuana during pregnancy are at higher risk for maladaptive social behaviors, cognitive problems, and psychomotor skills following birth (Gold & Dupont, 2008; Jones et al., 2015). They were also found to have lower reading comprehension skills at age 10 years (Goldschmidt, Richardson, Cornelius, & Day, 2004). This finding must be interpreted with caution, however, since there are numerous other variables besides maternal marijuana use that might also affect the child's reading comprehension skills at the age of 10. There is also evidence that children exposed to marijuana smoke in utero demonstrate abnormal tremors, startle reflexes, and eye reflex problems. Women who have smoked marijuana at least once a month are also thought to be at higher risk for premature labor, and for having children with lower birth weights, a higher risk of ventricular septal defects, and were smaller than normal for their gestational age (Bhuvaneswar & Chang, 2009). However, again, the separation of the effects of possible maternal cigarette smoking from maternal marijuana use makes these conclusions quite tentative.

In Jamaica, where heavy maternal marijuana use is common, researchers have failed to find any major differences between a group of infants exposed to marijuana in utero and a group of infants who were not exposed to marijuana during gestation (Dreher, Nugent, & Hudgins, 1994). Where the authors did find differences between these two groups, it was

¹⁹See Glossary.

noted that they could be attributed to the mother's social status, the number of adults living in the household, the number of other children competing for the mother's attention, and other environmental factors rather than maternal marijuana use.

It seems that some effects of maternal marijuana use will manifest shortly after birth or, in other cases, later in the child's life (Jones et al., 2015). Given the crucial role of anandamide in guiding neural growth and development during corticogenesis, it should not be surprising to discover that there is evidence of prefrontal lobe dysfunction in children exposed to marijuana in utero that did not manifest until the child was 6–9 years of age. But there is much to be discovered about the effects of marijuana use during pregnancy and the long-term outcome for the child exposed to marijuana in utero.

Marijuana and Breast-Feeding

There is only limited data to date about the impact on the infant of maternal marijuana use during breast-feeding (Metz & Stickrath, 2015). Before birth, the placenta provides some degree of protection against THC absorption. However, this compound is concentrated in breast milk, and research has revealed that the THC level in breast milk may be up to six times higher than that found in the mother's blood (Jones et al., 2015; Nelson, 2000). Given the small size of the infant, and the higher concentration of THC in the breast milk, the possibility exists that the infant will be exposed to significant levels of THC at a time when corticogenesis is still progressing. Thus, maternal marijuana use both during pregnancy and following birth is to be avoided.

Narcotic Analgesic Use During Pregnancy

Infants born to women who are misusing or addicted to narcotics²⁰ are unwitting participants in their mother's opioid use disorder (OUD), since the drugs easily pass through the placenta into the infant's blood. Following childbirth, these infants will be forced to go through the opiate withdrawal process. While limited exposure to opioids under a physician's supervision appears to present minimal danger to the fetus, long-term exposure to these compounds by a woman who is misusing or addicted to narcotics, even if interspaced with periods of abstinence when the mother is unable to

obtain drugs to use, does appear to hold the potential to harm the fetus (Jones et al., 2015). Notice that the word "potential" was used in the last sentence: Although the impact of some opioids on the newborn has been well documented, thus far there is little research into the possible long-term consequences of maternal opioid use during pregnancy (Bhuvaneswar & Chang, 2009; Jones et al., 2015).

Statement of the Problem

Estimates of the scope of maternal opiate misuse and addiction during pregnancy vary. Patrick and colleagues (2012) estimated that 3.39 of every 1,000 infants are born to mothers who are addicted to narcotics. In contrast to this conclusion, Tolia and colleagues (2015) reviewed the records from 299 neonatal intensive care units (NICUs) that collectively treated 647,845 infants from 2004 to 2013 and reported that there was an increase from seven admissions to an NICU for neonatal abstinence syndrome in every 1,000 births in 2004 to 27 admissions for this condition in every 1,000 births in 2013. This is a 300% increase in infant admissions to an NICU for treatment of their neonatal abstinence syndrome. Even this number might be an underestimate of the scope of the problem, since it is not unusual for the pregnant opioid user to switch to fentanyl prior to giving birth. The high potency of fentanyl makes it virtually impossible to detect on standard urine toxicology tests (Bhuvaneswar & Chang, 2009). On the basis of this data, it would not be unreasonable to estimate that an opiate dependent infant is born somewhere in the United States every half hour.

For women misusing opiates, many of the early symptoms of pregnancy such as fatigue, nausea, vomiting, pelvic cramps, and hot sweats, might be interpreted as early withdrawal symptoms rather than early symptoms of pregnancy (Bhuvaneswar & Chang, 2009; Kieser, 2005; "Medication-assisted treatment (MAT) during pregnancy—Part 1," 2009). Unless the woman were to confirm the possibility of pregnancy through one of the commercially available in-home pregnancy tests or medical examination, there is a danger that the woman dependent on opiates will attempt to self-medicate what is perceived to be early withdrawal symptoms by taking even higher doses of narcotics. This results in higher levels of fetal exposure to both the compounds being misused and the adulterants that are often mixed in with illicit drugs, and an increased risk for the infant to be exposed to one or more of the various infections that many opiate users acquire as a consequence of their OUD.²¹ Unfortunately, in many states the physician who identifies a woman who is

²⁰Or the very small percentage of infants born to women placed on long-term narcotic analgesic therapy for medical problems prior to childbirth.

²¹Discussed in Chapter 36.

pregnant and has an OUD is required to report the woman's pregnancy to the authorities, making many women hesitate to see a physician until the onset of labor (discussed earlier in this chapter, under cocaine).

Even under the best of conditions, pregnancy carries with it the potential for life-threatening complications for the woman. If she has a history of narcotics misuse, the potential for developing one or more of these complications is increased. Some of the medical problems that might develop during pregnancy in the woman addicted to narcotics are listed in Table 17-1 (Bhuvaneswar & Chang, 2009; Finnegan & Kandall, 2005, 2008; Kieser, 2005; Virani et al., 2009).

TABLE 17-1 Potential Complications for Mother and/or Infant When Mother is Opiate-Dependent

Potential Complications for Mother and/or Fetus
Anemia
Stillbirth
Breach presentation during delivery
Placental insufficiency
Spontaneous abortion
Premature delivery
Neonatal meconium aspiration syndrome (which may be fatal to the infant)
Amenorrhea
Postpartum hemorrhage
Neonatal infections acquired from mother
Lower birth weight
Neonatal narcotics addiction/withdrawal
Maternal diabetes
Increased risk of SIDS

If the mother should have, or acquire an infection during pregnancy, there is the additional risk that the fetus will develop the same condition. Such infections are potentially fatal to the fetus as well as to the mother. For example, approximately 30% of women who misuse illicit opiates and are pregnant develop the potentially fatal infection known as bacterial endocarditis. A high percentage of women who have viral hepatitis or HIV are thought to pass the virus on to their infant, either during gestation or during the process of giving birth, a process known as **vertical transmission**.

To limit the risk to both the mother and neonate, physicians now believe that the mother should *not* be withdrawn from opiates during pregnancy. It is recommended that the mother be stabilized on methadone or buprenorphine to normalize the intrauterine environment (Bhuvaneswar & Chang, 2009; Jones et al., 2015; Polydorou & Kleber, 2008).

This reduces the incentive for the mother to misuse other drugs, and there is evidence that suggests that children whose mothers had been stabilized on an opioid agonist experience longer gestation periods, and the mothers give birth to infants who are heavier at birth (Finnegan & Kandall, 2005). There is some evidence that infants whose mothers were stabilized on methadone had some visual problems following birth; however, the role of methadone in the development of such problems is still unknown (Hamilton et al., 2010). There is also an emerging body of evidence suggesting that with the opioid agonist buprenorphine for the control of maternal narcotic use, the infant might experience less distress during the neonatal opioid withdrawal process (Jones et al., 2010; Whitten, 2012a).

The neonatal withdrawal syndrome begins within 24–72 hours of birth (depending on the specific compounds being used by the mother) and has both an acute and extended phase. The *acute* phase of neonatal opioid withdrawal will last as long as 3–6 weeks.²² During this time, the infant will demonstrate such symptoms as (Finnegan & Kandall, 2005, 2008; Kieser, 2005) yawning, wakefulness, watery eyes, fever, shrill or high-pitched cry, stuffy/runny nose, salivation, hiccups, vomiting, diarrhea, poor weight gain, apnea, sneezing, tremors, and seizures. The second phase of neonatal withdrawal, the extended phase, might last for 4–6 months. During this phase, the infant might demonstrate such symptoms as restlessness, agitation, tremors, and sleep disturbance. These behaviors will add stress to the mother, who might be in the early stages of recovery from a substance use disorder, thus serving as a relapse trigger for the mother. Such infant behaviors might also interfere with the bonding process between mother and infant at a time when it is of critical importance (Kerrigan, 2008). As the information reviewed above suggests maternal opiate use disorders are quite dangerous for the infant.

Even with the best of medical care the infant going through the neonatal withdrawal syndrome is at risk for premature death, although this danger has dropped significantly since effective treatments for the condition were developed. Morphine is the most commonly used drug to assist the infant going through the neonatal withdrawal syndrome (Tolia et al., 2015). However, such medications as methadone or buprenorphine are used in some cases, and some physicians prefer to use a barbiturate during the neonatal withdrawal process to avoid possible withdrawal-related seizures (Kieser, 2005).

²²Depending on the opioids being used by the mother, (Bhuvaneswar & Chang, 2009) suggested that the first phase of the neonatal opioid withdrawal syndrome might last as long as 10 weeks.

For a variety of reasons, including hormone-related changes in the mother's body during pregnancy (Stout, 2009), the pharmacokinetics of many compounds are altered during gestation. The therapeutic half-life of methadone, for example, is reduced by about one-third in the mother, possibly requiring the use of higher doses of methadone to achieve adequate control of the mother's opiate-use urges. Thus, methadone stabilization should only be attempted by a physician experienced in this process. Following birth, the infant and mother can each then safely be detoxified from opiates.

Maternal Narcotics Misuse and Breast-Feeding

The narcotics, including heroin, do pass into breast milk, and thus the infant is exposed to the mother's narcotics use if she should breast-feed. During this phase of life, the infant's liver is still rather immature, theoretically allowing narcotics to build up in the infant's body between periods of active feeding. Theoretically, and with limited research support to date, prolonged periods of maternal narcotics use during breast-feeding might cause the infant to become sleepy, eat poorly, and possibly develop respiratory depression or an OUD from the trace amounts of opioids being used found in maternal milk (Jones et al., 2015).

Clinical and research evidence suggests that mothers using meperidine should not breast-feed, as this medication can cause the infant to become over-sedated (Hale, 2003). Research has also demonstrated that individual genetic variations in the infant might make the child exceptionally vulnerable to the CNS depressant effects of codeine (MacDonald & MacLeod, 2010). In addition to the infant's genetic heritage, their age is also an apparent factor in their vulnerability to codeine's toxic effects. This is because the infant's blood-brain barrier is still relatively immature, though it develops rapidly as the infant matures. Breast-feeding mothers who are using morphine under a physician's supervision can do so safely since only a minimal amount of morphine is concentrated in breast milk, and an even smaller proportion of the morphine ingested by the infant will actually reach the baby's circulation (Hale, 2003). The concentration of narcotic analgesics such as methadone in breast milk is less than 1% (Kieser, 2005) to 3% (Schottenfeld, 2008) of the mother's blood level. There is evidence that suggests that breast-feeding during the first days following birth may help the physical distress experienced by the infant going through the opiate withdrawal syndrome (Paradowski, 2008). This might reflect the soothing effects of touch during the process of breast-feeding.

It should be emphasized that the above information is an incomplete list of the possible impacts of maternal opiate use during pregnancy, and it should also be emphasized

that the above list does not attempt to address the problem of adulterants added to illicit drugs and their effects on the fetus. There is a great deal to be learned about these areas of medicine, which, unfortunately, are not afforded the same level of importance as other medical conditions.

Over-the-Counter Analgesics Use During Pregnancy

Aspirin

Aspirin has been found to cross the placenta, and thus enter the fetal circulation. Because of this, women who are or who suspect that they might be pregnant should not use aspirin except under a physician's supervision (Black & Hill, 2003; Wilson, Shannon, Shields, & Stang, 2007). Previous evidence indicated that there are risks to the use of aspirin during pregnancy, such as stillbirth and increased perinatal mortality. Further, aspirin use by the mother might be a factor in the development of fetal anemia, retarded intrauterine growth, and antepartum and/or postpartum bleeding, especially if the mother should ingest the aspirin the week prior to delivery. The risk of bleeding is not limited to the fetus, for aspirin will also interfere with the mother's ability to form blood clots, which may place her life at risk during labor and delivery. However, use of aspirin in low doses appears to be useful for many women in reducing the risk of preeclampsia, and seems to have little impact on the fetus or the infant after birth (Ahrens et al., 2016). Aspirin is generally not recommended during breast-feeding.

Acetaminophen

Physicians have recommended acetaminophen as an alternative to the use of aspirin during pregnancy (Black & Hill, 2003). However, there is evidence indicating that exposure to acetaminophen in utero increases the infant's risk of developing asthma in childhood (Beasley et al., 2008; Fan, Wang, Liu, & Li, 2017), as well as having an impact on neurodevelopment (Stergiakouli, Thapar, & Smith, 2016). Obviously, it will be necessary to examine this issue in more detail, but for now it is recommended that acetaminophen only be used under a physician's supervision.

Although low levels of acetaminophen are found in breast milk, there is no evidence at this time suggesting that this exposure has an adverse effect on the fetus, as long as the acetaminophen is used in appropriate doses. However, as always, the breast-feeding mother should contact her health care provider to discuss whether it is safe to use any medication.

Ibuprofen

There has been limited research into the effects of the pro-prionic acids on fetal growth and development (Black & Hill, 2003), although recent research indicates there may be a disruption in the endocrine system in utero (Maamar et al., 2017). Black and Hill (2003) recommended that ibuprofen and similar compounds be used during pregnancy only upon the advice of a physician, since there is some research data suggesting that these compounds may prolong labor, and possibly cause other effects on the developing fetus.

There is little evidence suggesting that ibuprofen enters human breast milk in sufficient quantities to cause problems for the newborn when used at appropriate dosage levels (Hale, 2003). However, as always, the breast-feeding mother should contact her health care provider to discuss whether it is safe to use any medication while she is breast-feeding.

Caffeine During Pregnancy

Although the impact on the development of the fetus needs more research, caffeine is a substance for which is important to consider only moderate use during pregnancy (Jones et al., 2015). Although research has not provided evidence to date that would indicate use should be eliminated, or that there are significant impacts on the neonate or the individual later in life, use of caffeine in large amounts has been linked to miscarriage (Jones et al., 2015). Given the lack of sufficient

research, caution should be used in ingesting caffeine during pregnancy and while breast-feeding.

Chapter Summary

If a woman with a substance use disorder were to become pregnant, the fetus that she carries would become an unwilling participant in the mother's SUD, since the majority of drugs cross the placenta and enter the fetal circulation. These compounds are often teratogenic, thus holding the potential to harm the fetus during gestation. This is especially true in the first trimester of pregnancy, which is a period of special vulnerability for the fetus. It is during this trimester that organ differentiation and the process of corticogenesis are underway. Disruption of these processes could potentially have lifelong consequences for the infant following birth.

If the mother were physically addicted to a compound(s), the infant might very well be born with a physical addiction to the same compounds. Indeed, if the mother were to have been drinking alcohol immediately prior to birth, it may be possible to smell alcohol on the infant's breath following delivery. The use of multiple compounds presents a special, substance-specific range of potential dangers to both the mother and the fetus, and even the over-the-counter analgesics have been found to have a significant teratogenic potential in some cases. The more significant of these risk factors, and the compounds that might cause these complications, are reviewed in this chapter.

Gender and Substance Use Disorders

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 18.1** Understand the lessons from history regarding gender similarities and differences for alcohol and drugs
- 18.2** Describe the impact of gender on the rehabilitation process
- 18.3** Understand the different effects of various compounds on women as opposed to men

Until very recently, drug abuse has been viewed as a marginal issue for women and portrayed largely as a male problem.

—Fox and Sinha (2009, p. 65)

Introduction

The issue of substance use disorders (SUDs) in women has long been overlooked by society. This oversight was fueled, in part, by the fact that for many years women were less likely than men to use illicit drugs (Anthes, 2010). However, women are closing the gender gap in the addictions. Epidemiological data suggests that 10.2% of men and 5.5% of women struggle with an SUD (Center for Behavioral Health Statistics and Quality, 2016); 6.5% of women acknowledge use of illicit drugs compared to 11.1% of men (Brady & Moran-Santa Maria, 2015). This gap is slowly growing smaller with each generation as the abuse of alcohol and illicit drugs has become more socially acceptable (Anthes, 2010). These statistics suggest that the SUDs in women are hardly a “marginal” issue. It is the goal of this chapter to try to dispel some of these stereotypes and examine the forces that help shape the growth of substance use disorders in women.

Gender and Addiction: The Lessons of History

It is unfortunately true that the lens of history distorts events in the distant past, and only rarely allows us to identify the parallels between a past situation and an evolving problem in time to avoid re-creating the mistakes that fill our history books. An example of how the lens of history distorts images from the past is the social belief that most of those who were addicted to “patent”

medicines at the turn of the 19th century were women. In reality, one-third of those persons who had become addicted to a patent medicine before the year 1900 were men, a fact that is rarely mentioned in the history books. This omission illustrates the double standard for men and women with an SUD that existed up until recently. Women who misused, or were addicted to, a drug were¹ subjected to a greater degree of social condemnation than men (Lynch, Potenza, Cosgrove, & Mazure, 2009). Paradoxically, their substance use disorders were viewed for many years as being less important than those of men (Cohen, 2000; Jerslid, 2001). The net result of this process is that information “on the natural history, clinical presentation, physiology and treatment of substance use disorders in women” has been lacking (Work Group on Substance Use Disorders, 2007, p. 44). Thankfully, the body of research is now growing (Bold, Epstein, & McCrady, 2017).

However, in the face of the earlier lack of research data, clinicians struggled to find effective treatments for the increasing number of women seeking substance use treatment. It takes time for treatment to catch up with the research evidence; only around 40% of rehabilitation programs provide any form of gender-specific treatment for individuals with an SUD, and many programs utilize a “one-size-fits-all” approach to substance rehabilitation. Regrettably, just as society started to develop an awareness of the scope of substance use disorders in women about a decade ago, advertising companies began to view women as an untapped market for alcohol use (Kindy & Keating, 2016). Increasingly, advertising companies target women with gender-specific advertisements. Alcohol use is portrayed as a sophisticated way to enjoy the company of friends, and its use is encouraged. This weakens the social prohibition against alcohol use, increasing the possibility that some women will engage in heavier alcohol use. A concurrent historical coincidence is that the other drugs that are misused have become more easily available, in spite of efforts to interdict them or to suppress the illicit drug trade. These factors all contribute to a growing substance misuse problem for women.

Statement of the Problem

For generations, society has struggled to understand the relationship between women and substance use. For generations, society’s response to the problem of substance use by women has been to hide the issue, protect the individual, or totally isolate her from social and/or family support (Blume & Zilberman, 2005a, 2005b; Cohen, 2000). This attitude is slowly changing, which is a welcome revision in social

attitudes, since it is estimated that 6.5 million women in the United States struggle with a substance use disorder (Tracy, Munson, Peterson, & Floersch, 2010). However, the change is not complete, and a double standard still exists: In the eyes of many, a woman who orders an alcohol-containing beverage at a public event will be perceived by both men and women as being more sexually available than a man who orders the same beverage, for example (Carr & Szymanski, 2011).

Social support systems, including peers, influence the individual’s substance use behaviors. If a woman has a close associate who drinks heavily, for example, she is herself more likely to both drink heavily and associate with those who drink heavily (Rosenquist, Murabito, Fowler, & Christakis, 2010). Age cohort membership is another factor that influences the individual’s substance use decisions, as reflected by the data in Table 18-1, which isolates substance use disorders in women by age cohort.

TABLE 18-1 Age Cohort Distribution of Substance Use Disorders in Women

Age Cohort	Percentage of Women Abusing Alcohol or Drugs
18–25 years	12.5%
26–49 years	6.5%
50 years and above	2.5%

Based on: Center for Behavioral Health Statistics and Quality (2016).

Substance Use Disorders in Women

Physicians and even peers do not always recognize the woman who has developed an SUD (Brady, Tolliver, & Verduin, 2007). It is not known whether this reflects the social denial that existed in earlier generations, a lack of recognition skills among physicians and friends, or possibly a combination of these two factors. This lack of recognition does leave the woman with an untreated SUD vulnerable to the direct and indirect negative effects of substance use. Women with an AUD, for example, are thought to be 23 times more likely to commit suicide than their nondrinking counterparts (Markarian & Franklin, 1998), while women with a drug use problem are 50–100% more likely to die as a result of their SUD when compared to women the same age who do not misuse chemicals (Fox & Sinha, 2009). Recent research indicates that women seeking treatment for cannabis use disorder have higher risk of suicide than men in their same age range seeking treatment (Foster, Li, McClure, Sonne, & Gray,

¹And, some would argue, women still are subjected to a greater degree of social condemnation when they have a substance use disorder.

2016), and that women within the Veterans Administration system with SUDs are at greater risk than their male counterparts (Bohnert, Ilgen, Louzon, McCarthy, & Katz, 2017).

The substance use disorders have never been a popular area for clinical research, and for much of the 20th century the limited research carried out in the field of the addictions focused exclusively on *male* subjects. The findings were then generalized to women with substance use disorders. Only now is it being acknowledged that hormonal, pharmacokinetic, neurochemical, and social factors alter a woman's ability to biotransform substances and affect her vulnerability to and recovery from substance use disorders (Brady & Moran-Santa Maria, 2015; Carr & Szymanski, 2011; Lynch et al., 2009). While gender-specific treatment programs are of value in the rehabilitation of the woman misusing substances, there is limited access to such programs in many parts of the country (Sinha, 2000).

The “Convergence” Theory

The “convergence” theory holds that the percentage of women with an SUD is slowly approaching that of men. There are many reasons for this convergence in substance use disorder rates. This theory is based on the mistaken assumption that substance use disorders in women at the start of the 20th century were rare, and only became more common during the last quarter of the past century. Yet, as was discussed earlier in this text, the majority of those who were addicted to a patent medication at the start of the 20th century were women, suggesting that the substance use disorders in women of that era manifested in different ways than was true for men. Further, given that a woman with a substance use disorder is less likely to be identified than a man with a similar SUD, this raises questions about the accuracy of the data on which the convergence theory is based.

Research data suggests that the time from period of first use to the development of physical dependence on a compound is *increasing* for women (Keyes, Martins, Blanco, & Hasin, 2010). Indirectly, the results of this study support the convergence theory: Like their male counterparts, women misusing substances are more accepting of recreational chemical use and trying more chemicals before potentially developing a substance use disorder. More evidence supporting the convergence theory might be found in research revealing that 8.1% of girls and 8.0% of boys will develop a substance use disorder at some point during adolescence (Upadhyaya & Gray, 2009). Further, the number of fatal car accidents involving 19–24-year-old women, an indirect measure of substance misuse, has increased in the recent past (Tsai, Anderson, & Vaca, 2010). Thus, there does appear to be evidence supporting the convergence theory that males

and females who misuse substances are starting to experience the negative consequences of their SUDs at similar ages, especially for younger age cohorts.

Does Gender Affect the Rehabilitation Process?

For a variety of reasons the answer to this question is: Yes! Women who enter substance rehabilitation are more likely to suffer from a psychiatric disorder that predates the development of their SUD (Brady & Back, 2008; Brady & Moran-Santa Maria, 2015). Further, sexual differences in brain development and function have been discovered, raising questions about the assumption that the neurological mechanisms of substance-induced reward are the same for men and women (Gur & Gur, 2016). Evidence suggests different brain activation patterns for each sex when exposed to the drugs that are misused (Pigott, Walker, Tietelbaum, & Lu, 2009). Women's brains appear to be more receptive to the rewarding effects of alcohol and drugs when blood estrogen levels are higher, making the reward system of the brain more responsive to stimulation (Anthes, 2010; Lynch et al., 2009). Such a monthly variation in reward sensitivity has not been noted in men with SUDs. The woman's body also appears to break down alcohol and illicit drugs in a slightly different manner than does the man's. The liver's P-450 metabolic pathway is involved in the biotransformation of approximately 80% of all drugs (DeVane, 2009). However, there are differences between the sexes in how the P-450 pathway functions, as well as wide interindividual variability, all factors that influence the biotransformation of various compounds (DeVane, 2009). Side effects of substances that are misused also tend to be different in men versus women, with frequency and severity being greater in women than in men, and women are more likely to experience side effects from some of the medications used in treating SUDs (Agabio, Campesi, Pisanu, Gessa, & Franconi, 2016).

There are neurological differences between how males and females respond to the various illicit drugs. It is known that the brain of a woman has a different pattern of dopamine transporter molecules in certain regions as compared to those of a man. This may alter the reinforcement potential of a given drug for women. Because of this process, it has been suggested that women might become addicted to a drug after less exposure to that compound than would be true for a man (Lynch et al., 2009). This theory is supported by the observation that female rats learn to self-administer drugs more rapidly than do male rats (Whitten, 2012a).

Then there are the social factors that influence how a person of either sex would fare in a treatment program.

Women are less likely than men to enter a substance rehabilitation program, in part because of social barriers that prevent them from doing so (Brady & Moran-Santa Maria, 2015; Gordon, 2007). Social stigmatization is another factor that affects how women and men view entry into drug rehabilitation treatment, although the stigma against SUDs in women is less in younger age cohorts (Brady & Moran-Santa Maria, 2015; Lynch et al., 2009). External barriers to treatment admission include having sole possession of children following divorce (or termination of a relationship), limited funding for treatment, or a spouse who also has an SUD, all of which might make recovery more difficult for the woman (Blume & Zilberman, 2004, 2005a, 2005b; Gordon, 2007). Although it is recognized that single parenthood is a barrier to treatment, few treatment programs have provisions for a woman who has custody of children (Blume & Zilberman, 2004; Ringwald, 2002).

Another barrier to treatment is that women who enter a rehabilitation program tend to have a smaller social support circle, often discovering that friends, family, employers, and society are less tolerant of a woman with an SUD than of a man with the same problem (Gordon, 2007). Intuitively, it would be expected that an important source of social support for the woman with an SUD would be her spouse or significant other. Consistent with this expectation is the finding that being divorced is a risk factor for SUDs in women between the ages of 30 and 40. Surprisingly, being *married* is a risk factor for women between the ages of 40 and 50! The reason for this discrepancy is not known, but it is hypothesized that it reflects age cohort differences. However, for both age groups, women with an SUD usually receive less support from their partner for efforts to recover than do men, increasing their potential for relapse (Green, 2006). It is for these reasons that marital therapy is often a useful adjunct to the woman's treatment program (Fals-Stewart, Lam, & Kelley, 2009).

Whereas men are most often introduced to drug(s) by peers, women commonly report that they were introduced to drugs by their partners, who then served as their main source of supply for the desired compounds (Blume & Zilberman, 2005a, 2005b; Small, Fast, Krusi, Wood, & Kerr, 2009). This pattern might extend to alcohol as well as illicit drugs, since there is less social stigma attached to a man buying a large bottle of liquor than to a woman doing so. This is one mechanism by which a woman's substance use disorder might be rendered "invisible" to others. Another manner in which SUDs in women are rendered invisible is that many women obtain their desired medications from physicians. Thus, they are not viewed by society as "addicts" but as "patients." Women also tend to progress quicker from first

use of a substance to using that substance regularly, and also to the first time entering treatment (Brady & Moran-Santa Maria, 2015).

Also, men and women tend to follow different pathways into treatment. Women are more likely to use the resources of a health care, clergy, or mental health professional at first, and only if their SUD is identified are they referred to a rehabilitation program (Blume & Zilberman, 2005a; Freimuth, 2005; Green, 2006). This tendency for women with SUDs to seek assistance from mental health professionals might be explained, at least in part, by the tendency for women to suffer from depression and/or anxiety disorders more often than men. These are conditions that frequently result in referrals to health care or mental health services (Blume & Zilberman, 2005a, 2005b; Dixit & Crum, 2000; Green, 2006). Women who have an alcohol use disorder (AUD) are seven times as likely to suffer from depression as are men with an AUD, for example (Brady & Back, 2008; Brady & Moran-Santa Maria, 2015). While these referrals to mental health professionals are useful, such "indirect" treatment of the SUD is rarely effective, and the substance use disorder itself must be addressed (Green, 2006). All of these details help explain, in part, why only 10.8% of those women identified as needing treatment received that treatment, while 89.2% did not receive treatment for their SUD (Center for Behavioral Health Statistics and Quality, 2016).

There are also gender-specific factors that aid, or inhibit, retention in treatment once a woman is admitted to a rehabilitation program. Greenfield (2010) identified some of these factors as (a) having a higher income, (b) being married, (c) being unemployed, (d) personal stability, (e) having a more stable family, and (f) having a lower combined burden of health, mental health, and social problems. Although at first glance factors (a) and (c) might seem to be contradictory, the loss of employment (especially in a high-status field) would serve as an incentive for the woman to successfully complete treatment or start a job search.

In contrast to women, men are more likely to enter treatment because of legal, marital, social, employment, or familial pressure. Like men, women who are referred to a rehabilitation program by the criminal justice system tend to have better treatment outcomes (Greenfield, 2010). After entering treatment, men and women relate to their SUD differently: Men tend to externalize responsibility for their SUD, while women tend to blame themselves. This is clearly seen in the observation that women with an alcohol use disorder have lower self-esteem as compared to men with a similar SUD (Cohen, 2000; Sinha, 2000). Another excellent example of how the dynamics of substance use disorders differ between men and women is that for the woman, the symptoms of depression are likely to serve as a relapse trigger for continued

further substance use (Brady & Moran-Santa Maria, 2015). Depression in the man misusing substances often triggers a reduction in substance use levels in an attempt to reduce his level of depression. This is not to say that men with substance use disorders might not suffer from clinical depression. Rather, this illustrates the different dynamics that are at work for men and women with concurrent SUDs and depressive disorders.

Another gender difference is found in how individuals misusing substances support their substance use. Males commonly support their drug use through discretionary spending funds, by drawing on family savings, or by the sale of drugs to others. Women who work out of the home frequently have to resort to spending savings or to prostitution to support their substance use.

Work, Gender, and the Substance Use Disorders

There is a complex relationship between the individual's work status and the SUDs. Women who are unhappy with their jobs, or who work in male-dominated professions, are prone to use alcohol more heavily (Jerslid, 2001). The importance of this observation becomes apparent when one stops to consider the fact that most women in the workforce are working below their capacity, often in low-status, high-frustration positions. While work potentially offers the woman increased social status, financial support, and improved self-esteem, all factors that help protect her against the development of an SUD, she might not feel challenged by the demands of her job.

Compared with males who misuse alcohol, women are unlikely to come to the attention of authorities (or employers) because of substance-related behavioral problems (Johnson, 2003). Since women tend to be underemployed, a woman's chemical misuse is less likely to result in under- or unacceptable job performance than is true for a male worker (Blume & Zilberman, 2004). Even if the woman's substance use is identified, the low-status jobs that some women hold do not generally allow for easy access to employee assistance program counselors, who often act as "gatekeepers" to treatment programs. Also, the threat of loss of employment for a woman in a low-status position is not as effective an incentive to enter treatment as it is for men. A woman may be able to simply quit her job if threatened with termination unless she should enter treatment, and find another job at the same level elsewhere. However, if the woman is the primary breadwinner in the family, then the referral to treatment is blocked by other barriers that stand between a woman and substance rehabilitation programs (discussed above).

Differing Effects of Common Drugs of Misuse on Women

For decades, much of what was assumed to be true about the effects of illicit drugs on women were extrapolated from studies using men exclusively, often men in Veterans Administrations hospital settings. The applicability of such research to women is certainly problematic. Further, since then, research has demonstrated gender-specific differences in alcohol and drug distribution and biotransformation. While scientists have long been aware that there are sexual differences in brain structure and function between men and women, how these affect the woman's responses to drugs has only recently been explored (Gur & Gur, 2017; Newman & Mello, 2009). The hormonal changes involved in the woman's monthly menstrual cycle have also been found to alter the woman's sensitivity to the effects of many drugs (Newman & Mello, 2009; Reed & Evans, 2009). A related issue is that research suggests that 20–40% of women of childbearing age utilize hormone-based methods of contraception. However, there has been very little research into how such methods of birth control might influence the woman's response to drugs that are misused (Erickson, 2007; Reed & Evans, 2009), as even the research on the interactions of contraceptives and prescribed psychotropic drugs continues to be lacking (Berry-Bibee et al., 2017).

There is also a growing body of evidence that suggests that some substance misuse by a woman might result in an earlier onset of menopause, given that it is already known that smoking is connected with earlier menopause (Fenton, 2015), although late menopause has been shown to be related to low and moderate alcohol use (Taneri et al., 2016). The possibility that premenopausal women might react to a drug in a different manner than postmenopausal women has not been explored. The issue of the differences between the factors that initiate, maintain, and assist rehabilitation from the drugs of abuse is thus quite complicated. In the next section, we will examine some of the known differences in the effects of various compounds on women as compared to men.

Alcohol Use Disorders in Women

The discussion of alcohol use disorders in women reflects a rather complex problem. Different age cohorts have different norms for alcohol use, and their peak period of alcohol ingestion varies from age cohort to age cohort. Women between the ages of 18 and 25 appear to develop an alcohol use disorder earlier in life than do women in the 26–49 age bracket (Center for Behavioral Health Statistics and Quality, 2016),

which might reflect the different norms for substance use between these two age groups, resulting in part from the shift in advertising in the past decade (Kindy & Keating, 2016). It is thus difficult to discuss the alcohol use disorders in women, since there are within-gender differences in the development of the AUDs.

Statistics demonstrate that women are less likely to develop an AUD than are men (Center for Behavioral Health Statistics and Quality, 2016; Erickson, 2007). However, the gender gap narrows in certain situations, such as for those experiencing significant adversity in childhood, which increases the risk of developing an AUD (Evans, Grella, & Upchurch, 2017). In those cases where the woman *does* develop an AUD, she is less likely to be identified as having this disorder. This is due in part to the fact that women tend to be solitary drinkers, and only rarely engage in the problematic behaviors that commonly are seen with male drinkers (Myrick & Wright, 2008; Nichol, Krueger, & Iacono, 2007). Solitary drinking by women might reflect the different dynamics of alcohol misuse between men and women. Men who misuse alcohol do so more to achieve the euphoric effects of alcohol, while the majority of women who misuse alcohol tend to do so to self-medicate emotional pain (Graham, Massak, Demers, & Rehm, 2007; Payne, Back, Wright, Hartwell, & Brady, 2009). Older women who live alone are at increased risk for alcohol misuse because of loneliness, depression, and suicide (Payne et al., 2009).

There is controversial evidence suggesting that *moderate* alcohol use may have a neuroprotective effect for women. Strandberg and colleagues (2008) concluded that women with a low to moderate alcohol intake level (defined by the authors as one to seven standard drinks a week) seem to demonstrate a significantly slower rate of cognitive decline as they age than do men. The authors speculated that the causal mechanism for the observed findings might reflect the protective effects of estrogen rather than the level of alcohol intake. However, they also did not rule out the possibility that the use of alcohol *in moderation* might be a contributing factor to the apparent protective effect of alcohol use in women. Sayed and French (2016) also found an impact for moderate alcohol use in women, with those identified as moderate drinkers self-identified as having better health than men or women who were former drinkers, nondrinkers, or light drinkers.

Unfortunately, women are more vulnerable to the negative effects of alcohol because of (a) lower body mass, (b) different fluid content, and (c) lower levels of gastric alcohol dehydrogenase in the stomach and liver (Brady & Moran-Santa Maria, 2015; Myrick & Wright, 2008; Payne et al., 2009). Women also have (d) a lower muscle mass to body weight ratio. As a result of these factors, the average woman

needs to ingest 40% less alcohol to achieve the same blood alcohol level as a man (Blume & Zilberman, 2005a; Collins & McNair, 2002; Reed & Evans, 2009). To further complicate matters, the normal variations in estrogen levels during the menstrual cycle affect the speed that alcohol is absorbed and its effects on the woman (Reynolds & Bada, 2003).

Physical Complications

It has been hypothesized that because of the process known as “**telescoping**,” women begin to experience physical complications from misuse of alcohol earlier in life than do their male counterparts (Blume & Zilberman, 2005a, 2005b; Brady & Back, 2008; Brady & Moran-Santa Maria, 2015; Myrick & Wright, 2008; Payne et al., 2009). Women are more sensitive to the toxic effects of alcohol on the striated muscle tissue than are men, for example (Blume & Zilberman, 2005a, 2005b). Such damage to the striated muscle tissue is seen after the average woman has ingested a lifetime total of about 60% of the amount of alcohol necessary to produce the same degree of muscle damage in men (Kinsella & Riley, 2007). It has also been found that the consumption of just two standard drinks per day increases the risk that the woman will experience cardiac arrhythmias such as atrial fibrillation (Conen et al., 2008). Qureshi, Dominguez, Choi, Jan, and Curhan (2010) followed a sample of 83,000 nurses and found that women who consume just two standard drinks a week appear to be at increased risk for developing psoriasis, for unknown reasons. Further, this risk appears to be dose-dependent, with those women who consumed larger amounts of alcohol reporting a higher incidence of psoriasis, again for unknown reasons.

Women with alcohol use disorders also appear to be at increased risk for central nervous system damage as compared with male drinkers, developing this damage after a shorter drinking history (Rourke & Grant, 2009). The pattern of brain damage is slightly different between the sexes. Hashimoto and Wiren (2007) discovered, for example, that female mice demonstrated a *higher* level of neuronal death during alcohol withdrawal than did male mice. It is not known whether this is true for humans as well, but these results were suggestive of a sex-specific pattern of neural death during the alcohol withdrawal process.

The average woman with an AUD who enters treatment will have more severe medical problems than the typical male who enters treatment for an AUD (Green, 2006; Sinha, 2000). The woman with an AUD, for example, usually requires just half the time to develop cirrhosis of the liver as a male, and the cirrhosis is more likely to prove fatal for the woman with an AUD than for the man (Myrick & Wright, 2008). Further, if the woman has a concurrent hepatitis C

infection, she typically will die 10 years earlier than a man with both conditions. Women with an AUD are vulnerable to reproductive system dysfunctions such as amenorrhea, uterine bleeding, dysmenorrhea, and abnormal menstrual cycles, as well as a reduction in ovarian size, infertility, and an increased rate of spontaneous abortions or miscarriages if she should become pregnant (Myrick & Wright, 2008; Payne et al., 2009; Schuckit, 2008a). They are also at increased risk for osteoporosis and breast cancer (Kovalesky, 2004; Myrick & Wright, 2008; Room, Babor, & Rehm, 2005; Sampson, 2002). It has been found that women taking birth control pills have a lower rate of alcohol biotransformation than women who do not use this method of contraception, extending the effects of alcohol in these women (Erickson, 2007). Finally, if the woman should suffer from a concurrent eating disorder, her alcohol use might exacerbate the electrolyte imbalances induced by the eating disorder, increasing the risk to her life (Benton, 2009).

Interpersonal Resources

Women with an AUD usually have a smaller social network than do men of the same age and substance use history, and they report that they receive less support for their efforts to abstain from chemicals than is typical for a man (Tracy et al., 2010). Women with an alcohol use disorder are *four times* as likely to be living with a partner who also misuses substances than are men. This appears to reflect the increased possibility that the woman will be financially dependent on her partner and thus less likely to seek a divorce from a partner with an SUD and who is also abusive (Blume & Zilberman, 2005a). Women who become the victims of interpersonal violence are five times as likely to develop a substance use disorder compared to women who are never exposed to these life experiences (Rees et al., 2011). Women who drank in isolation at home were found to be at increased risk for perpetration of interpersonal violence, possibly because of the lowering of inhibitions brought on by alcohol consumption (Mair, Cunradi, Gruenewald, Todd, & Remer, 2013). However, the greater the level of alcohol consumed by the woman, the greater the chance that her partner would become violent toward her (Mair et al., 2013). A **confounding variable**² that might influence the latter observation is that depressed women are prone to consume more alcohol per occasion, exacerbating the risk of alcohol-induced physical problems and IPV.

Women with an AUD tend to experience more social stigma, contributing to the problem of familial alienation

from the substance user (Brady & Moran-Santa Maria, 2015). Even if the woman should seek treatment, she is likely to encounter barriers to rehabilitation, such as child care, child custody issues,³ pregnancy-related issues, and having smaller social support systems. Many rehabilitation centers refuse to work with a woman who has children or who is pregnant, and few residential treatment programs have facilities for child care while the mother is in treatment.

A Positive Note

Although a great deal remains to be discovered about the impact of gender on the alcohol use disorders and their treatment, there are also hopeful signs emerging from the research data. Women, for example, appear to be more aware of their alcohol use disorders, and to respond more positively to interventions aimed at treating these problems. Thus, the treatment outcome for women with an alcohol use disorder is at least as good as, if not better than, for men with similar disorders who enter treatment (Brady & Moran-Santa Maria, 2015; Greenfield, 2010; Payne et al., 2009). Women who successfully completed treatment were found to be nine times as likely to abstain from recreational drug use as those who failed to successfully complete treatment (Green, 2006).

A Cautionary Note

Alcoholics Anonymous (AA) is often suggested as an adjunct to recovery. Within the framework of such a program, the woman is able to express her fears and concerns, or seek guidance from others or from her higher power, without having to fear repercussions, shame, or retribution (Hamilton-Mason & Melendez, 2011). Unfortunately, AA might also expose the woman to sexist mentality in a program based on confronting the perceived false pride on which addictions rest. Such an approach might not “be helpful to a woman who needs to build her self-esteem from the ground up” (Jerslid, 2001, p. 6), in part because, as a group, women tend to feel higher levels of shame than do men. It is for this reason that women are more likely to be solitary drinkers than are men with AUDs. But the AA program places great emphasis on uncovering the sources of shame, a characteristic that may make women feel uncomfortable or unwanted at these meetings (Blume & Zilberman, 2004; Jerslid, 2001). Complicating matters is the fact that women now start to drink at a younger age and to consume far greater quantities than did earlier generations (Greenfield, 2003; Grucza, Norberg, Bucholz, & Bierut, 2008; Sinha, 2000). Thus, the

²See Glossary.

³The woman’s AUD is often used against her in child custody disputes, for example.

challenge to AA at this time is both to eliminate the sexism inherent in the 12-step program, and to make the program relevant to all age cohorts of women. Whether this self-help program can accomplish this during the process of remaking itself to meet the needs of woman with AUDs in the 21st century remains to be seen. There are alternatives to AA, many developed specifically to address the needs of women (discussed further in Chapter 35).

Amphetamine Use Disorders in Women

Methamphetamine is but one of the family of the amphetamine compounds, but it has received the most publicity as a stimulant of misuse and thus will be the focus of this section. The ratio of male to female methamphetamine use is nearly 1:1 (Rawson & Ling, 2008); however, the dynamics of the methamphetamine use disorders are not the same for men and women. Men who use methamphetamine tend to be drawn to the drug for its euphoric effects, while women are most commonly drawn to methamphetamine because of its ability to induce anorexia and to self-medicate depression (Rutkowski & Maxwell, 2009). Research has found that women tend to find CNS stimulants such as methamphetamine more pleasurable during that phase of their menstrual cycle when estrogen levels are highest (Anthes, 2010). The differences in reproductive hormones also appear to make women more vulnerable than men to the addictive potential of central nervous system stimulants (Torregrassa & Kalivas, 2009).

Pleasure is not the only reason some women might misuse stimulants such as methamphetamine. Women who are forced to work in the illicit sex trade are at increased risk for methamphetamine misuse (at times, perhaps forced use) because of its ability to allow the woman to work longer hours (Rutkowski & Maxwell, 2009). Women who use cocaine or amphetamines are more likely to become the victims of interpersonal sexual violence (Gilbert, El-Bassel, Chang, Wu, & Roy, 2011). Seventy percent of women who use methamphetamine report a history of physical and/or sexual abuse in their lives (Rawson & Ling, 2008). This establishes a vicious circle in which the woman becomes addicted to an amphetamine compound such as methamphetamine, and in many cases is ultimately forced to work in the illicit sex trade to obtain the funds to support her addiction. The mild antidepressant effect of methamphetamine helps to explain the lure of this compound for women who have been abused or forced to work in the illicit sex trade. This might account for the fact that when an adolescent girl or young woman is

admitted to a substance rehabilitation program for a methamphetamine use disorder, she will usually report higher levels of use than is true for the average adolescent male.

Approximately one-third of women who use methamphetamine report having an anxiety disorder *before* they began to use methamphetamine, and two-thirds report symptoms of an anxiety disorder after starting to use methamphetamine (Brady & Hartwell, 2009). This raises the question of whether anxiety symptoms might not serve as a relapse trigger for the woman with a methamphetamine use disorder; however, research on this topic is lacking at this time. There is mixed evidence suggesting that women might be less vulnerable to the neurotoxic effects of methamphetamine due to the limited protective action of estrogen. However, Regner and colleagues (2015) found that the long-term misuse of amphetamines and cocaine appeared to be associated with a greater loss of **gray matter**⁴ in a number of regions of the brain associated with motivation and reward. The authors also noted that women addicted to CNS stimulants seek help for their SUD at a later point in life than do men with similar disorders. These gender-specific dangers are beyond the general physical and emotional risks of amphetamine use discussed in Chapter 8. Although there is still a great deal to be discovered about the effects of the amphetamine compounds on women, it should be clear from the information reviewed in this section that the dynamics and consequences of methamphetamine use by women are different from those for men.

Benzodiazepine Misuse by Women

There is little research data on the problem of benzodiazepine misuse by women or the pharmacokinetics of benzodiazepines in women, which is surprising in that the majority of prescriptions for benzodiazepines (BZs) are for women. When introduced, the BZs were marketed as useful in helping women deal with anxiety in the various medical journals in which the pharmaceuticals company paid for advertising. The advertisement usually began with a photo of a woman who was visibly distressed (sometimes with children or a work scene in the background), along with a second photo of the same woman smiling and interacting with her children and/or peers, suggesting that the benzodiazepine caused this transition. So prevalent is this mentality that in one study the rates of prescribing benzodiazepines to women with PTSD were shown to go up over a 10-year period, when during the same period of time the prescribing to men with PTSD went down (Bernardy et al., 2013).

⁴ See Glossary.

It is known that benzodiazepine blood levels in women using hormone-based birth control medications might be lower than normal because the birth control medication increased the speed of benzodiazepine biotransformation (Tatro, 2009). For unknown reasons, benzodiazepines that require conjugation as part of the *biotransformation* process,⁵ such as temazepam and oxazepam, have longer elimination half-lives in women as compared to men (Virani, Bezchlibnyk-Butler, & Jeffries, 2009). The benzodiazepines are used for a variety of issues in women, including PTSD and sleep disorders, but are most likely not working effectively (Bernardy & Friedman, 2016). However, there is a need for gender-specific research data on the problem of benzodiazepine misuse and addiction, and on the normal pharmacokinetics of the benzodiazepines in women.

Buspirone Misuse by Women

The misuse potential of buspirone has been debated, and at least a small group of individuals who misuse drugs look upon buspirone as their preferred drug. The personality characteristics of those who misuse buspirone or their motivation for misusing this compound have not been studied.

Cocaine Misuse by Women

The experience of cocaine use is not the same for men and women. The woman's gonadal hormones appear to influence her subjective response to cocaine (Newman & Mello, 2009; Reed & Evans, 2009). Higher progesterone levels have been found to mute the woman's sense of euphoria after using cocaine (Elton & Kilts, 2009; Lukas, 2006). Unfortunately, progesterone is involved in the maintenance of pregnancy,⁶ and this may add to the incentive for the pregnant woman to use *more* cocaine per episode, increasing the risk to both the mother and the fetus. A second danger is that since progesterone is a component in many hormonal-based methods of birth control, there is a danger that women using such methods of birth control might feel tempted to use more cocaine in an attempt to achieve the desired level of euphoria, again increasing her risk of an adverse reaction to the cocaine.

⁵ See Chapter 3.

⁶ The use of progesterone in birth control pills acts on the principle that this compound, normally found in high concentrations when the woman is pregnant, forces the body to assume that the woman is already pregnant. A fertilized egg will then be blocked from implanting itself in the wall of the uterus.

It has been observed that female rats appear to be willing to work harder for cocaine than are male rats, although the applicability of this finding to humans remains unclear. Human females who use cocaine appear to be at increased risk for developing the adverse effects of cocaine than is true for males who use cocaine. Some of the adverse effects of cocaine use by a woman include not just those identified in Chapter 9, but also include such problems as **galactorrhea**,⁷ **amenorrhea**, and infertility (Mendelson & Mello, 2008). However, clinical research does suggest that women who misuse cocaine develop a smaller number of cerebral perfusion defects and lower levels of damage to the frontal cortex than do males who misuse cocaine (Brady & Back, 2008; Brady & Moran-Santa Maria, 2015).

Women who use cocaine begin to do so at an earlier age than do males, and there is evidence that they are also more vulnerable to the addiction potential of cocaine (Lynch et al., 2009; McRae-Clark et al., 2016). Women may also be more vulnerable to stress, creating greater drug-seeking behavior in those already using cocaine (McRae-Clark et al., 2016). Women with cocaine use disorders tend to enter treatment at a younger age than their male counterparts. One surprising route of exposure to low levels of cocaine for a woman is through the semen of a male partner who uses cocaine (Karch, 2009). It is not clear at this time whether the exposure to the small amount of cocaine in the ejaculate could induce any form of physical reaction in the woman or serve as a relapse "trigger," although this is unlikely since the amount of cocaine in the semen would be quite small.

Hallucinogen Misuse by Women

Ecstasy (MDMA)

There is little research into possible gender differences in individuals' response to a hallucinogen such as MDMA, but there do appear to be gender differences in the metabolism of the drug (Mueller, Yuan, McCann, & Ricaurte, 2014). There is preliminary evidence suggesting that, for unknown reasons, women are more vulnerable to MDMA-related neurological damage than are men (Greenfield, 2003). However, the findings of a study by Medina, Price, Harper, Logan, and Shear (2008) would argue just the opposite. The authors attempted to examine the effects of MDMA on **executive functioning**⁸ and found that there was a dose-dependent relationship between the use of MDMA and lower working memory ability

⁷ See Glossary.

⁸ See Glossary.

scores. Although the authors found a significant gender effect, males who used MDMA were found to be more likely to demonstrate impulsiveness and impaired memory function as compared to females who used MDMA. Thus, the issue of whether there are sex-related differences in the pattern of neurological damage remains unclear at this time.

Yudko and McPherson (2009) suggested that males who are considered lower functioning appear to be at increased risk for MDMA-induced neurological deficits in the areas of verbal and visual memory, but not in women or in higher-functioning males, suggesting that premorbid level of function might be another variable besides gender that influences the impact of MDMA on neurological function. As this information suggests, there is a great deal to be learned about how MDMA affects both men and women; however, since this compound is illegal it is doubtful that such research will be forthcoming.

LSD and Phencyclidine

There has been virtually no research into the impact of LSD or phencyclidine use on the user's neurological function, or how these compounds might have different effects for men as opposed to women. Given a renewed interest in these compounds for psychiatric purposes (Schmid et al., 2015), there is the potential that future research will reveal gender differences.

Marijuana Misuse by Women

Statistically, women are more likely to begin to use marijuana at an older age than are men, with the mean age of first marijuana use being 17.6 years for adolescent girls as compared with 16.4 years for adolescent boys (McRae-Clark & Price, 2009). Men are about three times as likely as women to use marijuana daily; however, there is limited evidence suggesting that women progress to marijuana dependence more rapidly than do men (McRae-Clark & Price, 2009). There has been virtually no research into possible gender-based differences in the path to marijuana use. One study points to a different impact for males versus females who use marijuana on the structure of the brain, especially during the adolescent years (Lisdahl & Price, 2012), although possible gender-specific differences in the user's physiological reaction to marijuana have not been investigated.

Preliminary evidence does suggest that women who suffer from social anxiety disorder are more likely to turn to marijuana to self-medicate some of their distress than men, but further research is needed to explore this topic (McRae-Clark & Price, 2009). While marijuana use can induce

anxiety, especially in those inexperienced with marijuana use, it does not appear to do so more often in women than it does in men (Brady & Hartwell, 2009). At first the assertion by McRae-Clark and Price (2009) to the effect that 32% of women, but only 13% of men, experiencing marijuana-induced panic at some point in their marijuana-use careers would seem to contradict the assertion made by Brady and Hartwell (2009), but it is necessary to remember that there is a difference between the experience of *anxiety* and that of pure *panic* to see how both statements might be correct.

Those who misuse marijuana are at increased risk for depression, but the causal mechanism for this effect, or whether it is the same causal mechanism for men and women, has not been explored (McRae-Clark & Price, 2009). There has been virtually no research to determine whether hormonal-specific differences in the individual's physiological or subjective response to marijuana exist (McRae-Clark & Price, 2009). It is known that some women use marijuana to self-medicate premenstrual dysphoria, with some research pointing toward amelioration of symptoms (Newman & Mello, 2009; Slavin, Barach, Farmer, Luba, & Earleywine, 2017). There is preliminary evidence suggesting that men might be more sensitive to the positive effects of marijuana smoking than are women, but further research is needed to confirm this finding (Reed & Evans, 2009). As was discussed in Chapter 10, the use of marijuana often predates the onset of schizophrenia (Compton & Ramsay, 2009). However, women who used marijuana and then went on to develop schizophrenia did so about 4 years later than did men (Compton & Ramsay, 2009). Whether this is a reflection of some kind of marijuana-induced partial protection against psychosis or of another, undiscovered factor remains unknown.

Narcotics Misuse by Women

To date, only a handful of studies have examined the possibility that men and women will react differently to a narcotic analgesic. Neuropharmacologists have discovered that women appear to be slightly more sensitive to the analgesic effects of morphine as compared to men, but that they also seem to require more time before experiencing morphine-induced analgesia (Newman & Mello, 2009). Research based on animal studies suggests that female rats will self-administer more opiates when given the opportunity to do so than will male rats (Brady & Back, 2008). Additional animal study information indicates that females who use opiates and who discontinue use but go on to have children with males who have not used opiates seem to pass on a greater sensitivity to opiates in female offspring (Vassoler, Wright, & Byrnes, 2016).

The problem of prescription diversion is an ongoing issue, and the limited data that is available would suggest that whereas 9.6% of men 18–25 years of age have misused a prescription narcotic in the past year, only 7.5% of women in this age cohort have done so (Center for Behavioral Health Statistics and Quality, 2016). This incidence is less in those 26 and older, with 4.8% of men and 3.4% of women misusing a prescription narcotic in the past year (Center for Behavioral Health Statistics and Quality, 2016), which may relate to illicit drug use being less socially acceptable, or at least less frequently reported, in older generations. Further, the data suggests that approximately 57% of women who are addicted to opioids are addicted to prescribed medications as compared with 37% of men with a narcotics addiction (Back & Payne, 2009). Women are more likely to misuse opiate prescriptions as compared to heroin, with past month use of heroin at 0.1% of women compared to 1.6% for prescription opiates in a year (Center for Behavioral Health Statistics and Quality, 2016). There is strong evidence suggesting that the dynamics for prescription opioid abuse differs between the genders. Women who misuse prescription opioids tend to do so to cope with psychological distress, while men who misuse prescription opioids tend to have more legal and behavioral problems (possibly suggesting antisocial tendencies on their part) (Jamison, Butler, Budman, Edwards, & Wasan, 2010).

Women who misuse narcotics tend to begin to misuse of these compounds at an older age than do men, but the average woman will enter treatment for her SUD at about the same age or younger than males with OUDs (Hernandez-Avila, Rounsaville, & Kranzler, 2004; Zhou et al., 2017). This suggests that their opioid use disorder is “telescoped” into a shorter period of time as compared with males. While men are more likely to inject narcotics, women tend to use inhalation as the preferred method of administration, although there are exceptions to this rule. Finally, it has been found that women with OUDs were more likely to be involved in a sexual relationship with another individual who misuses drugs than were males with OUDs. More than half reported having received drugs as a present from their partner on occasion, a pattern rarely seen in male addicts with OUDs. There is also limited evidence that hormonal changes seen in the menstrual cycle might increase the woman’s sensitivity to pain, which might then become a relapse risk for her during the early stages of recovery. However, as noted above, there is a paucity of data concerning the opioid use disorders and gender,⁹ and much

to be learned about how gender affects the rehabilitation of those with OUDs.

Nicotine Misuse by Women

Perhaps the most significant fact about the nicotine use disorders in women is that, starting in the World War II era, the tobacco industry implemented a whole sales campaign designed to convince women to smoke cigarettes (Mukherjee, 2010). Regrettably, in spite of this decades-old campaign, the number of studies investigating the effects of cigarette smoking on women is limited and often contaminated by methodological errors. One such error is ignoring the woman’s physical, emotional, and victimization status (Blalock et al., 2011). The authors found that women who were physically or emotionally abused in childhood and who developed high levels of nicotine use found it more difficult to stop or reduce smoking when they became pregnant.

Another potential confounding variable is where in the menstrual cycle each participant was at the time of the study, since there are hormonal variances in how a woman’s body responds to and metabolizes nicotine. The method of birth control being used by the woman, if any, is another confounding variable, since hormone-based methods of birth control alter nicotine metabolism (Newman & Mello, 2009). However, in spite of the paltry database addressing the issue of cigarette smoking in women, researchers *have* found that women who smoke are as likely to die from tobacco-related illness as are men who smoke (Jha et al., 2013).

There are sexually dimorphic differences in the neural activation pattern of smoking between men and women. Fallon, Keator, Mbogori, Taylor, and Portkin (2005) examined the brains of men and women (smokers and nonsmokers) using **positron emission tomography (PET) scan**¹⁰ technology. They found a *decrease* in brain metabolism in the women in their study who were using transdermal nicotine patches, while the men in the study experienced an *increase* in brain metabolism when using transdermal nicotine patches. The exact ramifications of these findings remain unclear at this time. Caspers, Amdt, Yucuis, McKirgan, and Spinks (2010) found that middle-aged women who smoked demonstrated greater deficits in visuospatial abilities, cognitive processing speed, and executive function than did middle-aged men with a history of tobacco use or similarly aged women who never smoked cigarettes.

⁹If somebody is looking for a good master’s degree thesis or doctoral dissertation topic, you are welcome to develop this idea further.

¹⁰See Glossary.

To identify nicotine's differing effects on men and women, Sofuoglu and Mooney (2009) administered intravenous doses of nicotine to volunteer subjects, and found that the women in their study reported a stronger "rush" effect and were more likely to respond positively to a given dose of nicotine than were the men in the study. However, the women were also more sensitive to the negative effects of nicotine, according to the authors. The authors called for further research into how men and women might have different subjective effects from nicotine. There is also strong evidence that nicotine metabolism is different for men and women. Women appear to metabolize¹¹ nicotine more rapidly than do men, but they seem to be more sensitive to the rewarding effects of nicotine (Brady & Back, 2008; Reed & Evans, 2009). Men and women also appear to follow different pathways to nicotine use disorders. For example, adolescent girls are more likely to initiate tobacco use, and less likely to stop smoking, than are adolescent boys (Wunsch, 2007). Additionally, the reinforcing effect of nicotine has been shown to operate differently in males than in females (Jensen, DeVito, Valentine, Gueorguieva, & Sofuoglu, 2016).

Cigarette smoking is known to cause health problems specific to women. The average woman who smokes is thought to lose approximately 14 years of potential life due to health care problems either brought on or exacerbated by cigarette smoking. An excellent example of this is found in the observation that chronic obstructive pulmonary disease (COPD) appears to be more common in women who smoke as compared with men (Newman & Mello, 2009). Nonsmoking women tend to experience their first heart attack about 10 years later than do men, which is known as the "**myocardial infarction gender gap**." However, this decade of protection is lost if the woman smokes cigarettes (Herzog et al., 2007). Women who smoked were twice as likely to present to a hospital with symptoms of a specific form of heart attack¹² than their nonsmoking counterparts (Herzog et al., 2007). However, the authors also found that if the female who smokes were to stop smoking, her risk for cardiac disease dropped to that of her nonsmoking counterpart within 6 months, thus providing another incentive for a woman to quit smoking. In another study, Sandhu and colleagues (2012) examined the records of 101,018 women in the Nurse's Health Study and found that even smoking fewer than 14 cigarettes per day increased the woman's risk of sudden cardiac death, and that for every 5 years the women continued to smoke their risk of sudden cardiac death increased by 8%. The authors also found that with smoking cessation

the woman's risk for sudden cardiac death dropped, until at 20 years after the last cigarette her risk was the same as those of women her age who had never smoked.

Although cigarette smoking is an identified risk factor for strokes, Peters, Huxley, and Woodward (2013) found in their review of 42,401 individuals who had suffered a stroke that there do not appear to be any gender-specific differences for this risk. However, cigarette smoking is *the* most common cause of lung cancer in women (Newman & Mello, 2009). Cigarette smoking has also been identified as a risk factor for the development of various other forms of cancer in women, including cancer of the cervix, esophagus, pancreas, kidney, bladder, breast, and pharynx. If a woman who smokes should quit, her risk of cancer slowly declines over the next few years. There is even evidence that smoking cessation may result in a reduction in the size of some cancers for women after these tumors develop. Cigarette smoking has been identified as a cause of bone density loss in postmenopausal women (Carmona, 2004). Women who smoke cigarettes are at higher risk for developing rheumatoid arthritis, and as a group, women who smoke have been found to have less strength, and less psychomotor coordination, than nonsmoking women of the same age. The causal mechanisms for these effects remains unknown. Smoking is known to be a cause of reduced fertility in women, as well as fetal death or stillbirth (Carmona, 2004; Reichert, Selzer, Efferen, & Kohn, 2005).

Unfortunately, an emerging body of evidence suggests that "Big Tobacco" continues to focus advertising efforts on women and young girls ("'Deadly in pink' report targets Big Tobacco," 2009). At least two major cigarette companies, Philip Morris USA and RJ Reynolds Tobacco, have devised advertising campaigns designed to convince women that cigarette smoking is both fashionable and a sign of femininity ("'Deadly in pink' report targets Big Tobacco," 2009).

Smoking Cessation

There are several factors that influence the success of smoking cessation efforts in women that are not found in men. It has been found, for example, that the gonadal sex hormones involved in the woman's monthly menstrual cycle influence the subjective level of distress that she experiences in the early stages of smoking cessation (Newman & Mello, 2009). The possibility of postcessation weight gain often serves as a deterrent for smoking cessation efforts by women smokers (Williams et al., 2010). It is not known whether men anticipate the same degree of negative consequences associated with postcessation weight gain, and the role of gender-specific interpretations of post-cessation weight gain has not been explored. However, Williams and colleagues (2010) found that moderate physical exercise in their sample of women

¹¹ Since nicotine is not a prescribed substance, the term "metabolize" rather than "biotransformed" is being used.

¹² Technically known as the *ST-segment elevated myocardial infarction*.

who smoke who were attempting to quit appeared to reduce potential weight gain and appeared to provide at least temporary benefits by reducing withdrawal distress and weight gain, and increased the possibility of success on the part of the would-be for the woman who formerly smoked. The authors called for a larger study with a more diverse sample of women to determine whether this effect can be replicated.

The observed benefits of smoking cessation might differ for men and women. Admittedly, both groups benefit from smoking cessation, but the pattern of recovery follows a slightly different path for each sex. For example, there is evidence suggesting that women are less likely to benefit from the pharmacological effects of bupropion during smoking cessation (Lynch et al., 2009). Nicotine replacement therapies also appear less effective for women who smoke and attempt to quit with the assistance of this pharmacological support as compared to men. Finally, the factors that increase the individual's risk for relapsing are different between men and women. For example, women who are struggling with depression have been shown to be more likely to attempt smoking cessation, but are more likely to relapse during the first month as compared to men who are also struggling with depression (Cooper, Borland, McKee, Yong, & Dugué, 2016).

As this information suggests, there is a great deal to be discovered about how nicotine affects women, and whether smoking cessation treatment methods need to be altered to accommodate the woman's menstrual cycle status.

Other Compounds

Aspirin

Although aspirin is not a drug of misuse in the traditional sense, it is often used to provide a degree of protection against heart attacks and to treat a heart attack once it has started, as discussed in Chapter 16. However, there are gender-specific aspirin effects (Steinhuibl et al., 2009). Men who take aspirin to prevent cardiovascular events appear to have fewer heart attacks, while women who take aspirin appear to have fewer

strokes. The impact of aspirin on men versus women continues to be investigated (Chan et al., 2007; Mosca, Barrett-Connor, & Wenger, 2011).

There has been virtually no research into how the woman's menstrual cycle might influence her response to aspirin or the other NSAIDs.¹³

Chapter Summary

The relationship between gender and the substance use disorders (SUDs) moved through several stages in the 20th century. At first, it was hidden from polite society. If acknowledged at all, the victim was viewed as a "fallen" woman whose morals were suspect. As society moved into the middle of the 20th century, the face of SUDs changed, with physicians prescribing many drugs to women for various complaints such as anxiety or insomnia. This again rendered a large part of the problem of substance use among women hidden from society, and to a certain degree legitimized it, since the woman in question was only taking a prescribed medication, despite the potential for misuse.

In the last quarter of the 20th century, there was a growing awareness that a large percentage of women suffered from substance use disorders, as was true for men. When treatment was attempted, the treatment methods utilized were those that had been developed for males with SUDs years earlier, on the assumption that they would also work for women. This was a mistaken assumption, and by the last decade of the 20th century researchers started to understand that the course of the substance use disorders, the roads each sex traveled to develop their SUD, and the role the substance use played in their lives differed between men and women. In the last decade of the 20th century, researchers began to discover that there were subtle, and often significant, differences in how a given compound affected men and women. This chapter explored what is currently known about how gender changes the individual's response to various drugs, and the need for further research to help scientists better understand this phenomenon.

¹³ Discussed in Chapter 16.



CHAPTER 19

Hidden Faces of Substance Use Disorders

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 19.1** Understand the impact of substance use disorders on those who are homeless
 - 19.2** Identify the impact of substance use disorders on those in the military
 - 19.3** Understand the substance use disorders within the LGBT community
 - 19.4** Describe the impact of SUDs on those who have a disability
 - 19.5** Understand the impact of substance use disorders within ethnic minorities
-

Introduction

It would be nice if the substance use disorders (SUDs) would present with a singular set of signature symptoms, as this would make the identification of these problems easier. Many of the stereotypical images of a person with an SUD are familiar, such as the “skid row” alcoholic drinking a bottle of cheap wine wrapped in a plain brown paper bag. Another popular image is that of the male heroin addict, with a belt wrapped around his arm and a needle in hand, about to inject heroin into his arm. Such stereotypes heighten our awareness of the problem, while simultaneously blinding us to the fact that the SUDs do not always follow these pathways. Who, for example, would recognize the individual who is a white, middle-class, individual addicted to heroin working in an office setting, or the mother who is dependent on cocaine and who stops to buy some crack on the way home from a shopping trip? How many people would recognize the benzodiazepine dependency behind the smiling face of a day-care worker? It is the goal of this chapter to help the reader become aware of some of the hidden faces of SUDs.

Substance Use Disorders and the Homeless

It has been estimated that there are more than half a million individuals who are homeless in the United States (National Alliance to End Homelessness, 2016). Individuals make up 63% of this number, while families (usually headed by women) make up 37% (National Alliance to End Homelessness, 2016). Children or adolescents who are on their own make up 6.5% of the

individuals, whereas individuals who are chronically homeless make up 15% of the population, and families who are chronically homeless make up 2% (National Alliance to End Homelessness, 2016). The median age of homeless individuals is 50, which is predicted to continue to move higher with our aging population (Spinelli et al., 2017). Approximately 8% of those who are homeless are veterans of the U.S. armed forces (National Alliance to End Homelessness, 2016). Collectively, the substance use disorders comprise the most common category of psychiatric diagnoses for homeless persons (Nielsen, Rygaard-Hjorthøj, Elangsen, & Nordentoft, 2011). However, the incidence of SUDs does not always appear to increase after a person becomes homeless (Arehart-Treichel, 2004; Smith, Meyers, & Delaney, 1998). Indeed, the experience of losing one's home appears to act as an incentive for the individual to *stop* misusing chemicals, at least in some cases (Arehart-Treichel, 2004). However, some do indicate that the homelessness can be a cause of the SUDs, as the individual turns to substances to cope (National Coalition for the Homeless, 2009).

The role of the individual's substance use in the loss of one's home is complex, and there is not always a causal relationship. The causes of homelessness might be traced to (Joseph & Langrod, 2005) (1) high rates of poverty, (2) chronic unemployment or underemployment, (3) low-paying jobs, (4) loss of benefits, and (5) lack of affordable housing. It should be noted that these authors did not identify the SUDs as a major cause of homelessness, although substance misuse and mental illness do indirectly contribute to the problem of homelessness.

Alcohol is a common substance of misuse among the homeless, reflecting the general substance use pattern of this culture. In a recent study of those 50 and older, almost 65% of homeless individuals appeared to meet criteria for a moderate to severe SUD based on use of at least one illicit drug, whereas close to 26% appeared to meet criteria for a moderate to severe AUD (Spinelli et al., 2017). Methamphetamine use disorders are seen as a significant problem for the homeless (Rutkowski & Maxwell, 2009). However, it is not clear whether there is a causal relationship between the use of these chemicals and homelessness. If substance use rehabilitation is attempted, homeless individuals present special challenges to the treatment program staff. Issues such as medical problems (increased incidence of tuberculosis,¹ for example), keeping appointments, attending 12-step group meetings, or obtaining prescribed medications all become barriers to rehabilitation. If the homeless person also has a child, or children, these barriers to treatment are compounded by many orders

of magnitude. These are all social problems that must be addressed, but there does not appear to be any easy solution. Further research is needed regarding SUDs and those who are homeless, as they are underrepresented in the research thus far, which overall needs methodological improvements (Polcin, 2016; Priester et al., 2016).

Substance Use Disorders in the Military

The subject of substance use and SUDs in the military community is, in a figurative sense, like the elephant in the living room. The military culture is one that historically tolerates if not actively encourages alcohol use and misuse. However, in the mid-1970s substance misuse was recognized as a significant problem among active-duty military personnel, especially those assigned to combat assignments. Some units openly tolerated the misuse of chemicals even in combat areas, while other units discouraged substance misuse, at least in combat zones. Efforts were made to address this problem through urine toxicology drug testing and peer substance abuse counselors. One positive urine sample in many cases resulted in a referral to treatment, and a second resulted in dishonorable discharge from the military. These measures, plus the end of the controversial conflict in Vietnam and the end of the draft, contributed to a reduction in the level of substance misuse among active-duty military personnel.

However, the problem has not been eliminated: One study found that 20% of active-duty military personnel engage in heavy alcohol use, and that 47% engage in binge drinking (Institute of Medicine of the National Academies, 2012). Additionally, 32% of veterans have a diagnosis of an AUD, and 20% have diagnoses for other SUDs (Lan et al., 2016). Eleven percent of active-duty military personnel admitted to the misuse of a prescribed substance or an illicit drug (Institute of Medicine of the National Academies, 2012). It is possible that a number of those individuals who fell into the latter group also misused alcohol, as there is considerable overlap between alcohol and drug use. The situation has become so serious that the Institute of Medicine of the National Academies (2012) called for the hiring of mental health/substance treatment professionals with advanced training in the treatment of the substance use disorders. While this discussion has not provided an exhaustive discussion of the problem of the SUDs in the military,² it does

¹Discussed in Chapter 36.

²To save space we will not even attempt to discuss the problem of substance use disorders among dependents of military personnel.

underscore the fact that this is a problem. Substance rehabilitation professionals working with this population should obtain special training to develop the expertise necessary to be effective working with military personnel.

Combat Veterans and Substance Use Disorders

Combat veterans are a unique subpopulation of the military community. Participating in combat cuts across racial and other socially constructed lines, leaving the individuals with a common experience of having been in combat. It has been well established that people exposed to combat are at increased risk for substance use disorders (Santiago et al., 2010). It has been hypothesized that many veterans turn to alcohol as a way of self-medicating their combat-related traumatic memories, although alcohol use can also complicate the treatment of combat-related memories and posttraumatic stress disorder (PTSD), as well as traumatic brain injuries (TBIs) resulting from combat (Santiago et al., 2010). Additional recent information points toward the potential for stimulants (prescribed, taken as supplements for muscle enhancement, or illicitly obtained) to be a risk factor in exposing PTSD in combat veterans (Herbst, McCaslin, & Kalapatapu, 2017). Surprisingly, when substance use disorders are detected in returning veterans, referrals to treatment are rare (Santiago et al., 2010). Military members who might be aware of their problem perceive a number of barriers to appropriate treatment, including the lack of confidentiality within the military organization. In many cases, individuals pay for mental health or substance rehabilitation through private providers to avoid having their treatment for these disorders becoming common knowledge on base or post. Other barriers to care include schedule conflicts, the necessary assumption of child care responsibilities upon return from active service, and the lack of transportation to mental health treatment centers (Kim, Thomas, Wilk, Castro, & Hoge, 2010).

There are many reasons why combat veterans are at risk for substance use disorders. First, during combat individuals draw strength from their fellows and build a support system to help them cope, especially while in combat. However, units are often broken up and individuals are reassigned to other duties upon return from combat, separating the soldier from his or her support system. Multiple deployments to combat zones can further stress not only the individual's coping mechanisms but also the ability of the family to adapt (Darwin & Reich, 2011). It is possible that veterans and their families might turn to alcohol or illicit drugs as coping

mechanisms for combat-related stress conditions³ (Santiago et al., 2010).

Further, the age cohort from which enlisted individuals are drawn (ages 18–24) is also the age cohort most at risk for the substance use disorders. This might explain why individuals in the lower ranks are more likely to misuse alcohol than are noncommissioned and commissioned officers. The “culture of drinking” found in many military units also can contribute to a tendency for the individual to misuse alcohol rather than address their mental health problems. Finally, the military places emphasis on the individual being able to cope on his or her own, and instills a desire within the soldier not to appear “weak.” Unfortunately, untreated substance use disorders are associated with a higher tendency for the individual to be “separated” from the service under dishonorable circumstances, while untreated PTSD and anxiety disorders cause untold suffering not only for the veteran but also for the families who live with the veteran.

Substance Use Disorders in the Lesbian, Gay, Bisexual, and Transgender Communities

The clinical literature that explores the impact of substance use disorders on gay, lesbian, bisexual, and transgender populations has in the past mostly focused on the role of alcohol and drugs of misuse among men who desire sex with other men (Hughes et al., 2006). By contrast, the problem of alcohol or drug misuse among women whose sexual preference is other women, or among bisexual or transgender persons, had received relatively little clinical attention (Hughes et al., 2006; Shelton, 2011; Trocki, Drabble, & Midanik, 2009). It is estimated that sexual minority group members comprise between 2 and 9% of the general population (Kerridge et al., 2017; Trocki et al., 2009).⁴ Regrettably, clinical evidence suggests that the SUDs, including tobacco use disorders,

³It is not only the military member who experiences stress during a deployment to a combat zone. Family members must struggle to find financial resources to pay ongoing bills and maintain internal cohesiveness during a time of uncertainty about the well-being of the person on active duty.

⁴The lower estimates reflect those individuals who report a sexual identity that would place them in a sexual minority, while higher estimates reflect the percentage of the population that has engaged in behaviors typically seen in people who belong to a sexual minority subgroup (Trocki et al., 2009). Within this context, recreational drug use might provide an excuse for the individual to engage in behaviors he or she might not otherwise, blaming his or her state of intoxication (Cabaj, 2005).

are more prevalent in the lesbian/gay/bisexual/transgender (LGBT) population, with levels around 30% across all SUDs (Cabaj, 1997, 2015; King et al., 2003; Trocki et al., 2009). At present, the research picture has been greatly improved, with a significant amount of research on the amount of use and misuse, and the consequences of that use (Cabaj, 2015).

The prevalence of SUDs within the LGBT community has been viewed as reflecting an increased vulnerability to the SUDs for a variety of reasons. Individuals who announce their sexual orientation or even that they are questioning it at an early age tend to experience negative feedback from friends and family at a time when they are concurrently attempting to come to terms with their sexual identity. Alcohol or drugs offer the promise of temporary escape from this stress. Second, living on the fringes of a society that is, at best, only slowly coming to accept homosexuality as a possible variant of human relationships offers few opportunities for socialization within the general community. It is for this reason that the “gay” bar came to play such a central role in the LGBT community. It is a place where one might go to socialize without fear of ridicule, meet potential partners, or simply to relax. The gay bar also may play a major role in the process of learning about one’s sexuality and its implications for daily life.

Clinical research has described the problem of methamphetamine use in the LGBT community (Cabaj, 2015). It has traditionally been thought that the level of methamphetamine use within this subpopulation is higher than in the general population, particularly among gay individuals (Cabaj, 2015; Ling, Rawson, & Shoptaw, 2006). Gay or bisexual males are thought to use methamphetamine both for its arousal and its disinhibition effects (Rutkowski & Maxwell, 2009). Methamphetamine or other substance use among persons who identify themselves as being LGBT places most rehabilitation center staff at a disadvantage: There are fewer resources for therapeutic intervention with members of this community, and most staff members are uncomfortable working with this subpopulation, if only because they lack proper training to do so.

Research suggests that women who identify as lesbian or bisexual are more likely to drink, and that when they drink they tend to engage in heavy drinking more often than their heterosexual counterparts. Additional research suggests that these women are more likely to develop alcohol and drug use disorders,⁵ while men identifying as homosexual or bisexual are at greater risk for illicit drug use problems, although there are exceptions to this rule (Green & Feinstein, 2012). More than half of women with a same-sex orientation will have

an AUD at some point in their lives, a rate that is 5–7 times as high as the norm for women identifying as heterosexual (Cabaj, 2005). However, the methodology on which these estimates are based has been challenged (Cabaj, 2005). The early studies used samples drawn from volunteers at local gay bars, which may erroneously inflate the percentage of women with an apparent AUD (Cabaj, 2005). Statistically, those people most likely to frequent gay bars are going to be those people with an SUD, especially an AUD, resulting in an overrepresentation of persons with an SUD in samples drawn from these establishments. Further, emerging evidence suggests that it is inappropriate to include data from bisexual men or women with persons who prefer a same-sex orientation, because this appears to be a distinct subpopulation with different substance use patterns than those seen in persons with a same-sex orientation (Green & Feinstein, 2012). Preliminary evidence suggests that men and women who identify as bisexual are at increased risk for an SUD than persons with a same-sex orientation (Green & Feinstein, 2012); however, there is a need for more research into this topic.

There has also been little research into the health care needs of women who identify as bisexual or lesbian, and only preliminary research into the treatment method(s) that may be most effective for persons in the LGBT community (Cabaj, 2015; Shelton, 2011). Evidence suggests that women identifying as lesbian or bisexual are more likely to seek treatment than are gay or bisexual men. There are few dedicated treatment programs for LGBT clients, and those few programs that do exist are usually located in major cities where there is a significant LGBT population. This puts a geographic barrier in place for those who identify as gay, bisexual, or lesbian who live in more rural areas or smaller communities, who do not have access to these programs. There also has been a movement to establish special Alcoholics Anonymous (AA) group meetings oriented toward the specific needs of the LGBT population. It is not known whether such specialized groups are more effective for the individual than more traditional 12-step meetings (Boschert, 2010). Unfortunately, such specialized 12-step group meetings are also usually only found in major cities. Further, because formal religions often persecute or reject men and women who identify as preferring same-sex relationship, 12-step recovery programs can make members of LGBT community uncomfortable because of past negative experiences with spiritual communities (Boschert, 2010; Shelton, 2011).

There is much to be learned about the treatment of individuals misusing substances and who identify as LGBT. Few substance rehabilitation professionals take the time to consider how they feel about working with persons in the LGBT communities, which has the potential for a poor therapeutic alliance, if not treatment failure. There is thus a very real need

⁵Which might also include misuse of prescribed medications.

for substance rehabilitation professionals to be trained in and comfortable with working with those individuals identifying as LGBT.

Substance Misuse and Individuals with a Disability

It has been estimated that 12.6% of the U.S. population has a disability (Kraus, 2017). The most common disabilities are reviewed in Table 19-1 (Kraus, 2017).

TABLE 19-1 People Affected by the Most Common Forms of Disability in the United States

Form of Disability	Percentage of People
Hearing	3.6
Vision	2.3
Cognitive	4.8
Ambulatory	6.6
Self-care	2.5
Independent living	4.5

This data does not include every type of disability possible. However, it does illustrate the fact that a significant number of people in this country are living with a long-term disability. Unfortunately, there is at best a limited body of information about the relationship and form of the substance use disorders and the various forms of disability (Novotna et al., 2017). The available evidence would suggest that the SUDs are more common among people with a disability than in the general population (Corrigan, Bonger, Lamb-Hart, Heinemann, & Moore, 2005; Novotna et al., 2017; Pearson, 2009). This is clearly seen in the fact that 62% of those people who have a disability have an alcohol use disorder (Heinemann & Rawal, 2005), and that 23.4% of those with disabilities smoke, compared to 14.9% of those without disabilities (Kraus, 2017).

Unfortunately, social attitudes and a lack of training for health care professionals make working with a person with ability issues problematic (Novotna et al., 2017). The number of physicians who are fluent in American Sign Language (ASL) is quite limited, for example, leaving the physician dependent on a translator or family and friends of the individual to translate questions into ASL and the patient's response back into English. Because of time pressures, the physician might not ask the appropriate questions about the individual's substance use, or the translator (if a family member or friend) might censor the patient's responses. Even if a person with a disability is identified as having an SUD, treatment resources

are very limited. For example, many treatment programs rely not on professional sign language interpreters, but on friends and family members to carry out translation functions (Heinemann & Rawal, 2005). Even if treatment programs have videotapes of lectures that are closed captioned, more traditional treatment methods such as group therapy rarely involve interpreters, if only because of confidentiality issues. Individual therapy sessions are problematic if the therapist is not fluent in sign language, and those treatment centers that rely on family members or friends to interpret might cause the individual to censor their comments to avoid revealing embarrassing information to these people. The lack of staff who are fluent in ASL prevents the client from participation in informal give-and-take discussions outside of group or individual psychotherapy sessions, and can make the client feel isolated.

In contrast to this lack of treatment resources, *drug dealers* are quite happy to offer their "services" to those who are disabled. Some drug dealers have gone so far as to learn sign language to communicate with clients who are hearing-impaired, providing a service lacking in many rehabilitation programs. To complicate efforts at rehabilitation, many family members believe that the individual who is hearing-impaired (or people with other disabilities) are entitled to use recreational chemicals because of their disability. In this manner, significant others might overlook signs of an SUD that requires professional intervention. As this section has demonstrated, the physically disabled population forms a subgroup in the United States that is underserved and often hidden from view.

Traumatic Brain Injuries

The number of people living with the aftereffects of a traumatic brain injury (TBI) in the United States is slightly higher than the number of people living with a serious and persistent form of mental illness (Pearson, 2009), with 3.2 million people impacted by a disability resulting from a TBI (Whiteneck, Cuthbert, Corrigan, & Bogner, 2016). These facts often surprise students, as they are generally unaware of the impact of TBIs, or that the SUDs are a serious coexisting problem for persons who have suffered a TBI. Many of those who suffer a TBI did so while under the influence of one or more chemicals (usually alcohol) at the time of the injury. However, between 10 and 20% of those people who struggle to live with the impact of a TBI on their lives did not have an SUD at the time of their admission to a rehabilitation program (Pearson, 2009). These individuals apparently turned to alcohol or illicit drugs to self-medicate their frustration after reaching the point where hope for further recovery from the TBI is unrealistic.

Individuals who suffer a TBI often resort to denial about the role that their substances played in causing the

accident. Unfortunately, the TBI might make it difficult for the individual to *understand* the role that substances played in the accident that resulted in their TBI. Sometimes the individual will be reluctant to discuss what he or she believes are ways to cope with the aftereffects of the TBI because of the desire to hold onto these coping mechanisms. Thus, one challenge that faces the substance rehabilitation professional who works with patients post-TBI is the determination of whether their SUD (a) *predates* their injury, (b) was involved in and possibly caused the injury, or (c) developed after the injury. The role that a chemical plays in the individual's life in each of these three cases might be far different, and will influence the treatment goals.⁶ A confounding factor is (d) the degree of residual impairment that the individual struggles to adjust to after the TBI. Another confounding factor is that individuals with personality disorders make up a significant percentage of those who have suffered a TBI. This forces the rehabilitation professional to address the issues of the personality disorder while helping the person recover from and adjust to the aftereffects of the TBI, and simultaneously addressing the substance use disorder. Very few substance rehabilitation professionals have been trained to do all of these tasks (Corrigan et al., 2005).

Treatment guidelines for working with the patient with a TBI and who has an SUD are lacking, although there is evidence suggesting that duration of treatment is one predictor of treatment success (Corrigan et al., 2005). Financial incentives or job placement assistance might help motivate the individual to stay in treatment longer, and are especially helpful when working with personality disordered substance abusers who have suffered a TBI. Unfortunately, these individuals are perceived as a source of frustration for most treatment program staff, especially in those programs that do not normally work with patients who have suffered a TBI, who express the opinion that the person's needs would best be met "elsewhere." Except in very rare cases, "elsewhere" does not exist, and the person with a TBI who has been misusing substances is either ignored or referred to a suboptimal treatment center.

Ethnic Minorities and Substance Use Disorders

The topic of substance use disorders is fraught with metaphorical land mines that only serve to obfuscate the problem

rather than establish a basis for understanding. The charge has been made that President Richard Nixon's strategy for the "war on drugs" was based on the political goal of undermining support for the Democratic Party in the South (Hart, 2013). Congress also engaged in a form of racism by advocating one sentencing standard for possession of powdered cocaine and another for possession of crack. Although these are essentially the same compound, powdered cocaine is usually used by Caucasian, middle-class individuals, while crack is predominantly found in the inner cities. The most repressive recommendations for possession of a form of cocaine were applied to persons in the working and lower classes of the population of the South, who by coincidence were more likely to be Democrats rather than Republican Party voters.

Society has slowly started to accept that the substance use disorders in ethnic minorities might not follow the same pattern or trajectory as seen in the typical Caucasian who uses substances (Chartier & Caetano, 2010). However, substance rehabilitation professionals who work with members of various ethnic minority groups are faced with a conundrum: Rehabilitation programs appear to be as effective for ethnic minority members as they are for the general population (Blume & de la Cruz, 2005). However, ethnic minorities have limited access to general health care, social supports, or substance rehabilitation programs, and there is a paucity of research into the best modalities of treatment for minority group members (Niv, Pham, & Hser, 2009).

Another confounding variable is the process of acculturation for the individual (Collins & McNair, 2002; el-Guebaly, 2008). Each successive generation moves closer to the social norms of the dominant culture in the United States. Yet in so doing, members of many ethnic groups become more vulnerable to SUDs as existing cultural prohibitions against substance use are discarded in favor of those of the predominant culture (Collins & McNair, 2002; el-Guebaly, 2008). This introduces another confounding variable: intergenerational differences in the development of SUDs in the same minority groups as successive generations strive to adapt the behavioral rules of the predominant culture. There are also significant differences between various ethnic groups, preventing the development of a substance abuse rehabilitation model that might be applied to all ethnic minority groups in this country. With these observations in mind, the author of this text offers a *tentative* brief summary of the substance abuse patterns of some of the larger ethnic groups in the United States (Niv et al., 2009).

Native Americans

There is no standard definition of "Native American," and in some cases, the term American Indian or Alaska Native

⁶For example, a person who suffered a specific degree of injury while intoxicated would offer different treatment challenges than a second person who suffered the same degree of impairment and turned to chemicals as a way to cope with the anger and frustration over suddenly becoming disabled.

(AIAN) is preferred. Some researchers include Alaskan Natives with Native Americans, as if these diverse groups might share similar cultural and social traditions ("Alcohol and minorities: An update," 2002). The Native American population is not a single, cohesive group but a heterogeneous population of at least 2 million people belonging to between 200 (Franklin & Markarian, 2005) and 500 (Collins & McNair, 2002) different tribal units, or even up to 5.2 million when those who indicate their ethnicity with one or more other groups in addition to their Native American heritage (Norris, Vines, & Hoeffel, 2012). Even within the population of Native Americans there are many differences: Only about one-third of the identified members of the various tribes live on reservations (Beauvais, 1998). Just the fact that the other two-thirds live outside of an identified reservation makes them slightly different from those who live on the reservation, even if technically they are members of the same tribal unit.

Further, the different tribes have an estimated 200 distinct languages, as well as different cultural and social histories. This makes generalizations from research conducted on one tribal group to the next difficult, if not impossible. For example, in some tribes in the northeastern United States, 111 of every 1,000 people meet the criteria for a formal diagnosis of an AUD, while in some tribes of the Southwest, only 11 of every 1,000 members would qualify for the same diagnosis. Obviously, there are different forces at work within these different tribes to cause such discrepant rates of alcoholism. An example of the intergenerational variation within tribal units mentioned earlier in this chapter is seen in cases where younger members misuse alcohol and methamphetamine more often than their elders (Beauvais, 1998; Rutkowski & Maxwell, 2009).

While all of these issues make research into the interrelationship between the SUDs and tribal membership difficult, there are a few facts that are known. For example, the alcohol-related death rate due to liver disease for Native Americans is estimated to be almost five times that of Caucasians in the United States (Cunningham, Solomon, & Muramoto, 2016). There is also an apparent relationship between alcohol use and suicide within the Native American population (Crosby et al., 2009; Dillard et al., 2016). However, the long-held assumption that Native Americans consume more alcohol than Caucasians has recently been refuted in the research (Cunningham et al., 2016).

However, the Native American population presents with the highest rates of CNS stimulant misuse of all the various ethnic groups in this country (Gilder, Gizer, Lau, & Ehlers, 2014). Those who misuse stimulants in this subpopulation were found to be associated with lower familial income, lower levels of education, and an earlier age of initial

CNS stimulant use.⁷ Native American males have AUDs twice as often as do women ("Alcohol and minorities: An update," 2002). There are exceptions to this rule, however, as evidenced by the fact that approximately equal percentages of men and women in the Sioux Nation have AUDs (Collins & McNair, 2002). Nor can the use of a given compound such as alcohol be viewed in the same context in different Native American tribal units. There is also evidence that Native Americans might develop a substance use disorder for different reasons than people in the mainstream culture, although both groups might misuse the same chemical(s) (Schmidt, Greenfield, & Mulia, 2006).

There is little research about which treatment modalities might work best with a Native American who misuses substances (Rieckmann, Moore, Croy, Novins, & Aarons, 2016). Some data suggests that Native Americans misusing substances might have a better recovery rate if they are referred to a program that specializes in working with Native American clients (Schmidt et al., 2006). However, the number of such programs is quite limited, and a referral to such a specialized program is not always possible due to geographic and funding limitations. All too often the individual is referred to a treatment center that is poorly equipped to deal with Native Americans. Only 20% of substance abuse rehabilitation programs offer specialized components for Native Americans (Schmidt et al., 2006). Unfortunately, there has been little or no research into the relevance of the material contained in the "specialized component" to members of different tribal units. Further, there is little research into the specific treatment skills necessary to work with Native Americans. Markarian and Franklin (1998) suggested, for example, that Native Americans might withdraw into themselves if faced with high levels of confrontation, an observation that has implications for rehabilitation programs serving this population. Rehabilitation center staff working with this population must be sensitive to the cultural differences and beliefs of these clients, both within a single tribe and between tribes.

One popular misconception that cuts across tribal boundaries is that Native Americans are more sensitive to the effects of alcohol than are members of other ethnic groups. There is little factual evidence to support this belief (Caetano, Clark, & Tam, 1998). Further, although it is widely believed that European explorers introduced alcohol to Native Americans, there is historical evidence suggesting that at least some tribes used alcohol in religious ceremonies, as a medicine, and as a way to prepare for warfare before the arrival of European

⁷Raising the question: Was their lower educational level a factor in the initiation of the CNS stimulant use or the result of it?

explorers (Collins & McNair, 2002). So at least some tribes were aware of alcohol and its effects before the arrival of European explorers, and much of what we thought we knew about the SUDs in this population has been shown to be inaccurate. There is so much to be discovered about the history of alcohol use within the Native American population, the treatment modalities that are most effective in the rehabilitation of individuals misusing substance, and what treatment methods might be counterproductive in the treatment of Native Americans with an SUD that arguably most health care professionals are ill-trained at best to work with Native Americans.

Hispanic (Latino) Clients

It is estimated that approximately 16.7% of the entire population of the United States is Hispanic as of 2015 (U.S. Census Bureau, 2016). However, there is a problem in speaking of a single “Hispanic” or Latino population in that individuals normally classified as Hispanic in surveys might in reality come from any one of 20 or more different countries (el-Guebaly, 2008). About 60% of the Hispanic population traces their roots to Mexico, 15% came from Puerto Rico, 5% from Cuba, and the rest from various other countries. Each of these social groups has different cultures and different attitudes toward alcohol and drug use (Franklin & Markarian, 2005). To illustrate the differences between these subgroups, on occasion a word that holds one meaning in one Latino subgroup will carry a different, possibly socially offensive, meaning in another subgroup. Yet these different subpopulations are all lumped together under the rubric of “Hispanic” or “Latino” by researchers, a mistake that introduces many variables into research on treatment effectiveness that are not controlled for at the time of the research study.

Traditionally, alcohol use, especially heavy alcohol use, is seen as a male activity within the Hispanic cultures (Collins & McNair, 2002), and Latinos do have higher rates of SUDs compared to Latinas (Alvarez et al., 2016). However, there are significant differences in the prevalence of substance use between the various Hispanic subgroups noted above. Eighteen percent of Mexican Americans are considered heavy drinkers, for example, while only 5% of Cuban Americans engage in heavy alcohol use (Collins & McNair, 2002). In both subgroups, it is rare for a woman to use alcohol, and an even smaller percentage engage in heavy alcohol use (Collins & McNair, 2002). Yet Latinas often enter treatment with greater levels of severity than males of Latino descent (Alvarez et al., 2016). The need for specialized treatment resources for the Hispanic population exceeds demand: Only about one-third of substance abuse rehabilitation programs offer specialized components for Hispanic

clients (Schmidt et al., 2006). Even if the individual does have access to a program with a specialized component for the Hispanic cultures, there are many barriers to treatment: Language barriers, perceived stigma, childhood custody, and legal concerns over immigration status, in addition to financial and geographic issues, all limit access to treatment even if such resources are available (Alvarez et al., 2016; Conner, Le Fauve, & Wallace, 2009; Niv et al., 2009). If the individual misusing substances is the mother, provisions must be made for child care and education while she participates in treatment, and adequate financial resources must be found for the treatment program and support the family while she is in treatment. All these factors conspire to make participation in treatment virtually impossible for the mother. If the person misusing substances is a family member other than the mother, then the financial burden still might prevent that person from entering treatment.

Individuals who are Hispanic also often experience longer delays in receiving care for their substance use disorder, receive less active treatment for their SUD, and are less likely to be referred to residential treatment programs for their SUD (Dunigan, 2009; Niv et al., 2009). These delays result in increased risk to life: Approximately 29% of individuals who identify as Latino who ended their lives were legally intoxicated at the time of their death, for example (Crosby et al., 2009). This figure does not include people of Hispanic heritage who consumed some alcohol prior to their suicide attempt but who were not legally intoxicated at the time of their death. Thus, there is a need for substance abuse rehabilitation programs to develop not just a sensitivity for working with Hispanic clients, but also an awareness of the differences between various Hispanic subgroups and equality in treatment services offered.

Asian Americans

This term is also misleading: Depending on the researcher and the definitions used, this term might include Chinese Americans, Filipino Americans, Asian Indians, Korean Americans, Japanese Americans, and Vietnamese Americans, people from Hawaii, Micronesia, and Polynesia (“Alcohol and minorities: An update,” 2002; Conner et al., 2009). Each of these subgroups has its own diverse culture, traditions, and in many cases languages, yet in many research studies they are lumped together as Asian American (Franklin & Markarian, 2005).

Depending on the Asian American subpopulation under discussion, women are more likely to abstain from alcohol or drink only on special occasions than are their male partners. However, even this rule must be tempered with the observation that women from various subgroups have widely

disparate alcohol use patterns. For example, only 20% of Korean American women admitted to the use of alcohol on occasion, while more than 67% of Japanese American women admit to using alcohol at some point (Caetano et al., 1998). In recent research, methamphetamine was the main drug identified as problematic among these subgroups, for both genders, followed by alcohol and heroin (Han, Lin, Wu, & Hser, 2016). There is to date little research about the needs of these subgroups, or the treatment methods that might be most effective when they are admitted to a rehabilitation facility (Han et al., 2016).

African Americans

Until recently, there had been a paucity of research addressing substance use disorders in African Americans, but there is a growing body of literature addressing the issue of substance use disorders in this subpopulation. Such research has found that African American males with alcohol use disorders were more likely to initiate heavy drinking later in life than Caucasian males, but were more likely to experience physical complications from alcohol use earlier in life (Edlund, Booth, & Feldman, 2009; Franklin & Markarian, 2005). Additionally, research indicates that discrimination does impact the frequency of illicit drug use for some African Americans (Carliner, Delker, Fink, Keyes, & Hasin, 2016).

To complicate matters, there is also evidence suggesting that intergenerational differences in substance use patterns within the African American culture exist. African American women in the 18–29 age cohort are significantly more likely to have an alcohol use disorder than are their older peers, with 3.8% of the younger age cohort meeting diagnostic criteria for an AUD as opposed to only 2.1% for older age groups (Payne, Back, Wright, Hartwell, & Brady, 2009). African Americans frequently follow a different path into a rehabilitation program. For example, African American women are 10 times as likely to be involved with the court system for a substance-related problem than are Caucasian women (Schmidt et al., 2006).


Regrettably, there is evidence to suggest that African Americans with an SUD will receive a different quality of treatment than Caucasians with a substance use disorder

(Schmidt et al., 2006). African Americans tend to remain in treatment for shorter periods of time as compared with Caucasian clients, for example, and are more likely to be discharged before successful completion of the rehabilitation program (Niv et al., 2009). The possibility exists that African Americans with an SUD are less likely to perceive a need for treatment than are Caucasians (Edlund et al., 2009), and this may be combined with a lower quality of treatment services. As this data suggests, there is much to be discovered about this subpopulation and the treatment methods that might be most effective in helping individuals from this subpopulation recover from substance use disorders.

Chapter Summary

While this chapter does not discuss the relationship between every subgroup of those who will use and misuse substances, it has attempted to demonstrate there are many subpopulations within this country about which very little is known in terms of the factors that might initiate or maintain a substance use disorder, or the treatment methods that might be most effective with each subpopulation. All too often, studies that have been conducted in this area have utilized exclusively male samples, the result being that virtually nothing is known about the factors that might initiate or maintain the substance use disorders in subpopulations.

The stereotypical image of what a “typical” person with a substance use disorder is like often blinds us to the fact that there are many hidden subpopulations with their own unique cultures and histories. The substance use trajectories for persons from each subgroup might be significantly different from members of other subgroups, and may even vary greatly within each subgroup. The avenues toward the initiation of, maintenance of, and recovery from substance use disorders also differ from one subgroup to the next. These subgroups are rarely recognized by treatment professionals as being different. Their needs in rehabilitation programs and the barriers to treatment that they encounter are often ignored when they are referred to a standardized “one-size-fits-all” treatment program.



CHAPTER 20

Substance Misuse by Children and Adolescents

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 20.1** Understand the concerns regarding the impact of SUDs in children and adolescents
- 20.2** Identify why children and adolescents may misuse substances
- 20.3** Understand the levels of concern for adolescent substance misuse
- 20.4** Review some of the screening and assessment tools used with children and adolescents
- 20.5** Understand diagnostic considerations for children
- 20.6** Review the consequences of SUDs in this age group for various substances
- 20.7** Understand rehabilitation options for adolescents

Introduction

It is often surprising for students to learn that *childhood* as we understand the term is a recent social invention. Two and a half centuries ago, children were viewed as little adults and were frequently treated as such by the society in which they lived. In the 19th century, childhood was viewed as a brief period of rest and discovery before the individual was expected to assume the responsibilities of adulthood. By the end of the first decade of the 21st century, developmental psychologists, neurologists, and pediatricians all agreed that childhood and adolescence are periods of “rapid physical, cognitive, emotional, social and behavioral changes” (Upadhyaya & Gray, 2009, p. 421), separate from adulthood. At this point, however, agreement among various researchers breaks down. A consensus has yet to emerge about such basic issues as when childhood ends or adolescence begins. If one accepts the onset of puberty as the definition of the start of adolescence, as Windle and colleagues (2009) suggested, one is then faced with the exceptional interindividual variability of the onset of puberty. Some children reach this developmental milestone as early as 10 years of age, while others do not do so until several years later.

The onset of puberty itself is a stressor that can contribute to substance use disorders (SUDs). Children who start puberty early are often ill at ease around their peers because of their increased physical size, and they may start to associate with older adolescents who approximate their own

physical stature but are emotionally more mature.¹ Children who start puberty later than their peers are vulnerable to feelings of inferiority as they (literally) look up to their physically more mature friends. During this time, the individual moves from elementary school to middle or “junior” high school, a process that brings with it stage-specific developmental demands. It is important to keep in mind the fact that the developmental changes in childhood and adolescence are tied to the individual’s age, but that they are not synonymous with the aging process (Masten, Fode, Zucker, & Spear, 2009). Children or adolescents of the same biological age might be working their way through different stages of psychosocial growth (Masten et al., 2009). Disruptions in the developmental trajectories of children and adolescents hold the potential for mild, moderate, or severe intensity depending on the individual’s support system and resilience, placing stress on the child or adolescent, who is also simultaneously facing questions about substance use or abstinence.

To understand child or adolescent substance use disorders, it is necessary to place the individual’s substance use behavior in the context of his or her level of cognitive and social maturity. These chemicals offer the promise of pleasure, and often of belonging, to the child or adolescent at a time when they are possibly ill-prepared to understand the hidden dangers associated with the use of these substances, or they believe that these consequences will never happen to them. Substance rehabilitation professionals thus need to be aware of the differing needs and potentials that children and adolescents possess and how substance use by children and adolescents is a complex problem that is influenced by a variety of factors. While the topic of child and adolescent substance use and misuse is worthy of a book, in this chapter we will briefly examine the complex problem of child and adolescent substance use disorders.

The Problem of Substance Use and Substance Use Disorders in Childhood and Adolescence

Substance use disorders in childhood and adolescence have been a social problem for generations. In the 19th century, children, especially those who were in middle childhood or older age cohorts, were viewed as economic assets to the family and were expected to contribute to the family’s financial resources (Charlesworth, Wood, & Viggiani, 2013).

¹ A relative term in the sense that a 13-year-old is hopefully cognitively and emotionally more mature than a 9-year-old.

During this period, alcohol dependence was rampant among children and young adolescents in England (Wheeler & Malmquist, 1987). However, starting in the late 19th century, a social reform movement was begun, seeking to protect children and adolescents from what was viewed as a work environment that was detrimental to their health, as well as from the perceived ravages of alcohol or illicit drug use in these age cohorts. This social welfare system coincidentally developed during the arrival of the industrial age, during which mass production displaced “hundreds of thousands” (Epstein, 2013, p. 18) of children and adolescents from the workforce.

Possibly as a result of this juxtaposition of economic and social forces, an educational system that was open to all children² replaced the older system, under which only privileged children or adolescents were able to go to school. While these social changes altered the environment in which underaged substance use flourished, it never really disappeared, and the economic cost to society is estimated to be \$62 billion a year (Spoth, Greenberg, & Turrissi, 2009).

Research has repeatedly demonstrated that children begin to form personal attitudes toward and expectations about alcohol and later drug use early in life. By preschool, children have at least a rudimentary knowledge of alcohol, its effects, and social norms that govern its use (Zucker, Donovan, Masten, Mattson, & Moss 2009). There is limited anecdotal evidence of substance misuse by children; however, the substance use disorders most commonly develop during adolescence (Crowley, 2007; Zucker et al., 2009).

A Complicating Factor

Students are often surprised to learn that “childhood” and “adolescence” are social constructs, the definition of which varies from one culture to another³ (Epstein, 2013). A century and a half ago children were viewed as essentially being little adults,⁴ who entered an apprenticeship to learn a trade during childhood and from which they would graduate years later as young adults. Other children entered the workforce

² In an apparent attempt to avoid charges that the public schools were in violation of the separation of church and state mandate of the Constitution or of religious bias, most public schools avoid the topics of religion or spirituality. Unfortunately, this is the phase in life in which the child’s moral and spiritual growth begins its most rapid development. This avoidance might contribute to the increased use of alcohol and illicit drugs in the later childhood and adolescent years.

³ The proof for this statement is found in the simple question: When does infancy end and childhood begin? The answer to this question varies from culture to culture.

⁴ And in the eyes of the legal system, often punished as if they were adults.

at an early age.⁵ They did not keep the money they earned, but would use it to help support their family.⁶ In a beautiful example of social evolution, the concept of adolescence emerged, and with it expectations placed upon the adolescents not to work on a full-time basis⁷ but to use this phase of life for socialization, vocational training, and participation in educational experiences. An unintended side effect was the production of an age cohort that has relatively few responsibilities, with a comparatively great deal of free time and large amounts of disposable income.

In the post–World War II era, for example, it was possible for the individual to enter the workforce upon graduation from high school and assume the responsibilities of full adulthood (Furstenberg, 2010). The shift in economic emphasis from manufacturing to one of skills and technology during the last half of the 20th century brought with it a reduced need for persons who seek to enter the workforce with only a high school diploma (Furstenberg, 2010). Concurrently, the educational qualifications necessary for entry-level positions in most professions were raised to a vocational-technical school diploma or a college degree,⁸ or even an advanced degree. Even with a college degree, many young adults are finding it difficult to find a full-time position. To survive financially, many young adults are forced to work multiple part-time jobs. Again, in an example of social evolution, Masten and colleagues (2009) suggested that a new phase of life, “emerging adulthood,” be used to describe these individuals (p. 5). This might account for the phenomenon of holding people back from full participation in adult society, which contributes to the depression, defiance, and anger typically associated with adolescence (Epstein, 2013).

Having established that childhood and adolescence are social constructs, we are still forced to integrate the ongoing problem of the substance use disorders into these socially defined phases of life. This is not an easy task. It is recognized that prolonged substance misuse in either childhood or adolescence can influence, or even block, the growth and development that society defines as the norm for each stage of

growth. The various drugs that are misused also potentially alter the neurological development seen in childhood and adolescence, and their use frequently prevents the individual from moving from one developmental stage to the next. With prolonged use, alcohol and the various drugs of misuse also inhibit the individual’s emotional and physical growth, possibly establishing the foundation for the problems mentioned by Epstein (2013).

The impact of alcohol or illicit drugs on socially defined growth norms are influenced by such factors as (a) the age at which the substance use is initiated, (b) the intensity with which a chemical is misused, (c) the duration of substance misuse, and (d) whether such substance misuse results in unanticipated physical injury (such as involvement in an alcohol-related accident, for example). The implications of the SUDs are still being explored and integrated into the gestalt of these social constructs, an exciting process in which we are participating even as you read these words.

Lamentably, much of the research conducted on adolescents in the past 60 years is of limited value in understanding the current childhood and adolescent age cohorts.⁹ The age at which children enter puberty in the 21st century is markedly lower than it was a century ago (Masten et al., 2009; Spear, 2010). Early puberty has been identified as a stressor for the individual, even if this is becoming the developmental norm in society. Those individuals who enter adolescence at an earlier age are more vulnerable to the development of a substance use disorder than are their peers who reach puberty at a more appropriate age (Brown et al., 2009; Gunn & Smith, 2010; Wagner, 2009).

Scope of the Problem of Substance Use in Childhood and Adolescence

Childhood Substance Use Patterns

The database on the scope of child substance use behaviors is exceptionally limited at best (Donovan, 2013; Gunn & Smith, 2010; Millar, 2009; Zucker et al., 2009). Donovan (2013) observed, for example, that current studies do not include children under the age of 12 years. This is unfortunate, because Minkoff (2008) suggested that for many children, the initial substance use may occur well before the age of 9, possibly as early as 6 years. These figures appear rather daunting, but they

⁵There are memorable photographs of children working alongside their fathers in a coal mine or in a factory setting in the late 1800s and early 1900s, for example.

⁶The truth of this statement is found in the observation that in over 100 different cultures, what we would classify as children and adolescents work alongside their elders, learn from them, and through their work contribute to the family’s resources.

⁷In contrast to the expectation in past eras that the adolescent’s earnings would be used to help defray the family’s finances, today’s adolescents are often allowed to keep their earnings for personal use.

⁸A significant percentage of the jobs available today did not even exist 40 years ago. The professions of “information technology specialist” or “web page designer” spring to mind here.

⁹Each generation grows up in a separate technological and social matrix. Imagine, if you will, a world without cellular telephones, text messaging, or the internet, for example.

are based on the assumption that *any* alcohol use by children is illegal. Keep in mind the following: In at least 37 states, parents can provide alcohol to children under the age of 21¹⁰ in certain situations (Hingson, 2010; Ingraham, 2016). Sometimes parents or other adults will allow a child to sip an alcoholic beverage to satisfy their curiosity about its effects. In some states, it is legal to allow alcohol to be served to a child under 18 years of age if a parent or responsible adult is present. It is not known whether the child might interpret survey questions about drinking as being applicable because of the controlled use of alcohol under adult supervision. If a child admits to the limited use of alcohol at the age of 12 years, is this evidence of an alcohol use problem or of parental permission for that child to drink under carefully controlled conditions? The conclusions by Zucker and colleagues (2009), who suggested that few children under the age of 9 consume alcohol without their parents being aware of the fact, would suggest the latter. If this is true, then the question of parental complicity in their children's alcohol use is raised.¹¹ With these problems in mind, consider that Johnston, O'Malley, Miech, Bachman, and Schulenberg (2017) reported that 61% of the high school seniors surveyed have used alcohol at least once. There has been a gradual downward trend in the number of high school seniors reporting alcohol use in the past decade, as reflected in Table 20.1 (based on Johnston et al., 2017).

Children and adolescents are adept at finding compounds with psychoactive properties, including many compounds normally thought of as cooking spices (Bourgeois, Parhasarathi, & Hategen, 2014). Unfortunately, there has been

virtually no research into their psychoactive, toxicological, or pharmacological effects (Bourgeois et al., 2014). There is evidence that alcohol advertisements are broadcast at times when children or adolescents are most likely to be watching television, an observation that, if proven, raises disturbing questions about the role of advertising in the development of alcohol use disorders in these age groups (Chung et al., 2009). Beer is the most commonly consumed form of alcohol, although there is growing evidence that liquor is becoming increasingly popular with adolescents because it is more easily hidden from adults by mixing it with soft drinks (Centers for Disease Control and Prevention, 2007). There has been a very slight, gradual, downward trend in the level of high school student alcohol use. However, as the above data demonstrates, alcohol use is prevalent by the time of graduation from high school.

Whether it is sanctioned by a parent or not, the percentage of children and adolescents who report alcohol use at some point in their lives increases between the eighth and twelfth grades (Johnston et al., 2017). The authors found that 22.8% of eighth-grade students surveyed reported having used alcohol at least once, as opposed to 61.2% of twelfth-grade students. Adolescent curiosity might account for some of this reported alcohol use, although a high percentage of the reported alcohol use reflected recreational drinking. Alcohol use is certainly the most common form of substance use for adolescents and contributes to traumatic injuries in this age group. One in 10 adolescents who drink will drive after consuming alcohol, placing the adolescent and pedestrians, passengers, and other drivers at potential risk.

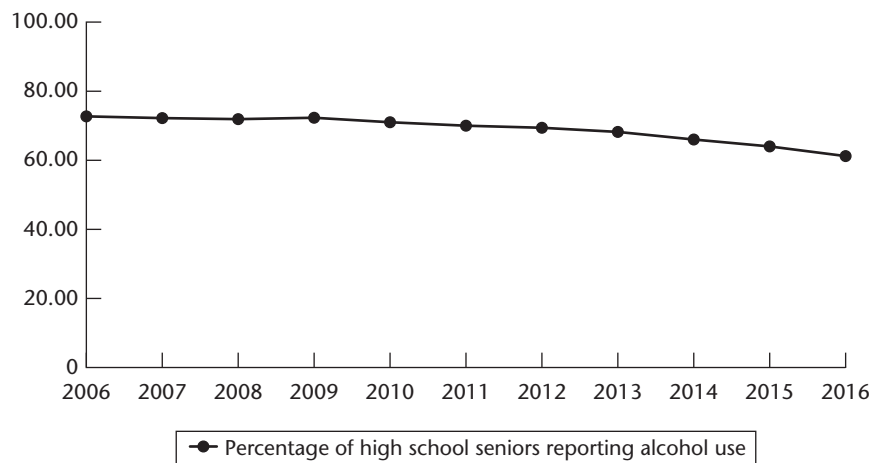


FIGURE 20-1 Percentage of High School Seniors Reporting Alcohol Use at any Point in Their Lives.

¹⁰ It is up to the reader to consult with an attorney to determine what laws apply to the geographical area where the student lives.

¹¹ Which in some states might be interpreted as a form of child abuse.

One-third of drug-related visits to local hospital emergency room for persons in the 12–20 age cohort involved alcohol, with males being the most likely to require such treatment (SAMHSA, Office of Applied Studies, 2010). Seventy percent of such visits involved alcohol alone, while 30% involved alcohol and/or drugs, according to the report. The danger of adolescent drinking and driving is seen in the fact that teenaged drivers who have a blood alcohol concentration (BAC) of 0.08%¹² or higher are 17 times more likely to die in an alcohol-related motor vehicle accident than if they were sober.

Adolescent Substance Use Patterns

The database for adolescent substance use behaviors is marginally better than that for childhood alcohol and drug use. In one of the few realistic surveys of adolescent substance use, the Substance Abuse and Mental Health Services Administration (SAMHSA, Center for Behavioral Health Statistics and Quality, 2017) estimated that in 2016:

- 7.9% of 12–17-year-olds used illicit drugs in the past 30 days.
- 6.5% of 12–17-year-olds had used marijuana in the past 30 days.
- 0.4% had misused prescription drugs in the past 30 days.
- 0.6% had used some kind of inhalant in the past 30 days.
- 0.5% had used a hallucinogen in the past 30 days.
- 0.1% had used cocaine in the 30 days preceding the survey.

A useful data source about adolescent substance use are surveys conducted on student populations from various schools. However, many high-risk students do not attend classes, or at the very most do so on an inconsistent basis, and thus may never take such a survey. For example, Hispanic students who use alcohol frequently are more likely to drop out of school (Windle & Zucker, 2010). Adolescent substance use patterns reflect geographic location, regional availability of certain substances, peer group pressure(s), parental guidance (or lack thereof), current substance use trends, etc. Thus, the information that follows should be accepted as conservative estimates of the scope of the problem of illicit drug use by adolescents.

Marijuana continues to be the illicit compound most commonly used by high school seniors, making up the greatest portion of the illicit drug use by this research sample (Johnson et al., 2017). It will be interesting to see the impact of legalization on marijuana usage on those under the age to use marijuana legally, as the trend of usage had been gradually going down, as can be seen in Figure 20-2.

A growing problem for adolescents is the diversion of prescription medications for illicit use (Millar, 2009). When asked which prohibited substance was easiest for them to obtain, 15% of the students surveyed said beer, while 23% said marijuana, although the misuse of diverted prescription medications, especially opioids, has become more common (Johnston, O’Malley, Miech, Bachman, & Schulenberg, 2017; Madras, 2010; Wunsch, 2007). Approximately 25% of high school students report having used a medication prescribed for somebody else, usually sharing that medication with a person of the same gender (Eaton et al., 2010;

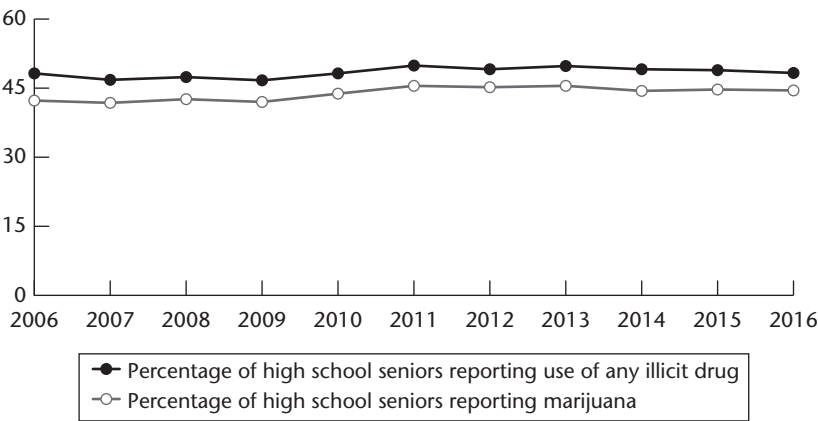


FIGURE 20-2 Comparison of Adolescent Marijuana Use Against Total Illicit Drug Use.

¹²The blood level of alcohol used by all 50 states define intoxicated driving.

Miller, 2007). This switch in substance patterns might reflect the fact that adolescents who use alcohol or drugs often do not realize that these compounds can be both addictive and carry a high potential for overdose and possible death (Heymann, 2008; Madras, 2010). Adolescents often believe the myth that you can only become addicted to narcotic analgesics if you inject them. Thus, they believe that it is safe to use intranasal methods of administration, and then as their use evolves into an addiction they are forced to turn to injected narcotics to achieve the same results once achieved with lower doses or less intense methods of use (Collins & Leak, 2008; Marsch et al., 2005).

The diversion of CNS stimulants such as methylphenidate or one of the amphetamine compounds is also of growing concern, with 23% of adolescents admitted to a substance rehabilitation program admitting to the misuse of such compounds (Croft, 2006). As the number of prescriptions for CNS stimulants aimed at controlling the symptoms of ADHD increases, there is evidence of an increasing problem of stimulant abuse and diversion as well (Setlik, Gond, & Ho, 2009). The usual methods of misuse are by oral ingestion or intranasal use. In contrast to the above information are those compounds that might be administered intravenously. The intravenous use of any compound is so rare during adolescence that it should automatically be seen as a sign of a serious SUD.

Although adolescent substance use, if only on an experimental basis, is the norm rather than the exception, the distinctions between substance *use*, *misuse*, and *dependence* are very indistinct. Since alcohol and illicit drugs are illegal by definition, many clinicians believe that *any* substance use during childhood or adolescence is a sign of a serious problem. Other clinicians maintain that *experimental* substance use, especially of alcohol and marijuana, is just one aspect of adolescence (Greydanus & Patel, 2005; Kaminer & Tarter, 2004). The essential questions Greydanus and Patel (2005) suggest are “not whether most teenagers will use drugs, but which one’s they try” (p. 392), how often they do so, and when. Given this information, how does a parent determine what is experimental substance use as opposed to problematic use? In the next section, we will examine this question in more detail.

Why Worry About Substance Use Disorders in Childhood and Adolescence?

There are many reasons why the use of alcohol or drugs by children or adolescents is of special importance. First, there is good evidence that adolescents who smoke cigarettes are

50% more likely to develop an alcohol use disorder later in life (Gruzca & Bierut, 2006). Further, the SUDs are the leading cause of mortality for older adolescents, contributing to accidental death, suicidal thoughts and attempts, interpersonal violence, motor vehicle accidents, and the problem of individuals having unprotected sex (Kaminer & Buckstein, 2005; Patrick & Schulenberg, 2014; Miller, Levy, Spicer, & Taylor, 2006; Shepard, Sutherland, & Newcombe, 2006; Windle et al., 2009). Cumulatively, the estimated financial cost of alcohol-related rape, homicide, assault, larceny, burglary, motor vehicle theft, loss of employment, and medical care for underaged drinkers to society is \$3 per mixed drink, a cost that far outweighs the estimated 10 cents in taxes generated by that drink.

Adolescent substance use is also part of the health care problem facing the United States. Complaints of chest pain are the third most common reason why adolescents seek health care, for example. Research has demonstrated that 17% of adolescents in a hospital setting for assessment of chest pain had ephedrine in their urine in spite of often strident denials that they had abused this compound (James et al., 1998). The cost of the medical evaluation for a possible cardiac condition in the adolescent is both labor- and resource-intensive. If the adolescent’s chest pain is found to reflect not a cardiac disorder but unsuspected drug use, then these health care resources become part of the health care problem in the United States.

The Neurological Factor

Since the turn of the century, neuroscientists have determined that childhood and adolescence are periods of dynamic growth in the central nervous system (CNS) (Giedd, 2015; Hopson, 2013; Jorgensen, 2008; Parekh, 2006; Wetherill & Tapert, 2013).¹³ Some of the neurological changes initiated in adolescence do not reach fruition until well into early adulthood. Because of this ongoing neurodevelopmental process in the CNS and an innate drive for novelty and to learn, children and adolescents assess risk and differently than do adults, a process that causes them to underestimate the dangers associated with unknown situations (Szalavitz, 2012). Children and adolescents also have different biological responses than adults to alcohol or the drugs of misuse (McVoy & Findling, 2009; Zimmer, 2011). All of these differences suggest that children or adolescents using such substances are not miniature adults

¹³ The topic of developmental neurology is rather fascinating. However, it lies outside the scope of this chapter, and must be referenced only in passing. The reader is referred to any of a wide range of textbooks on the subject if she or he is interested in learning more about this subject.

for whom the same treatment protocols will work, but a distinct subpopulation for whom new treatment paradigms must be developed.

The effects of the various drugs of misuse on childhood or adolescent neurological maturation is dependent on (a) when the individual begins to use the compound(s) in question, (b) the duration of use, (c) the intensity of use,¹⁴ (d) the frequency of use, and (e) the individual's emotional maturity level, among other factors. Adolescence is a time of rapid neurological growth: The development of what is known as the "gray matter" in the human brain normally peaks at about the age of 11 in girls, and approximately a year later for boys (Windle et al., 2009). After that point, there is a gradual reduction in the volume of gray matter as the brain eliminates neural pathways¹⁵ that are unused or redundant (Giedd, 2015; Meyers & Dick, 2010; Windle et al., 2009). It is during adolescence that the highest levels of **white matter**¹⁵ development is seen (Giedd, 2015). Binge drinking in adolescents can induce altered fiber coherence in this white matter (McQueeney et al., 2009). Even moderately heavy alcohol use during adolescence, such as that necessary to produce a hangover in the drinker, may affect neurological growth (Squeglia, Spandoni, Infante, Myers, & Tapert, 2009). To date, a similar process among adult drinkers has not been identified, suggesting that this sign of neurological injury might be stage-specific to adolescence, although the implications of this alteration in gray matter fiber coherence are not known at this time.

The hormonal changes that begin during puberty initiate neural changes in the brain's reward system that achieve full expression during adulthood (Zimmer, 2011). However, this is an uneven process, and the cognitive assessment and control systems of the brain lag behind the growth in the brain's reward system during adolescence (Dobbs, 2011; Eagleman, 2015; Giedd, 2015; Hopson, 2013). This might be why the adolescent brain is more sensitive to the rewarding effects of alcohol (and possibly the illicit drugs) than the adult brain (Rutherford, Mayes, & Potenza, 2010; Spear, 2010). A region of the brain known as the **ventral striatum**,¹⁷ which is strongly interconnected with the limbic system, appears to amplify the rewarding effects of environmental stimuli for adolescents (Zimmer, 2011).

In contrast to how adults attend to and interpret novel stimuli through the prefrontal regions of the cortex,

adolescents appear to attend to the same stimuli through the activation of the **amygdala**¹⁸ region of the brain, which is involved in emotional information processing (Thatcher & Clark, 2008). Thus, adolescents process information differently than do adults, reacting emotionally when an adult would be more rational¹⁹ (Giedd, 2015). Since memories associated with strong emotion, such as the reward cascade, initiate by substance use, are stronger, and are more deeply entrenched in the mind, substance abuse during adolescence exposes the user to the risk of establishing very strong positive memories of the effects of a compound of misuse and positive associations between substance use and specific locations, making it more likely that she or he will want to repeat that experience later (Brenhouse & Anderson, 2008).

When compared with adults, adolescents appear to experience less sedation from a given dose of alcohol (Strauch, 2003; Upadhyaya & Gray, 2009; Varlinskaya & Spear, 2006). This might explain why extreme binge drinking, defined as consumption of 10 or more drinks in a row, is a growing problem for high school seniors (Patrick & Schulenberg, 2014). The lack of sedation could potentially overwhelm constraints against engaging in high risk-behavior(s) such as engaging in unprotected sex, driving while under the influence of mood-altering chemicals, etc. One reflection of the increased incidence of engaging in high-risk behaviors while intoxicated might explain why substance abuse in adolescence, especially early adolescence, raises the individual's lifetime risk for an SUD (Madras, 2010; Rosenbloom, 2005). The risk of developing an alcohol use disorder is 4–6 times higher for the adolescent who begins to drink before the age of 15 as compared with the individual who begins to drink at the age of 21 (Madras, 2010; Meyers & Dick, 2010). This increased risk level is reflected in the finding that almost half of those persons who become alcohol-dependent do so before they are legal adults and entitled to buy alcohol (Nelson, 2007). In contrast, only about 20% of those individuals who develop an AUD at some point in their lives do so after the age of 30 (Nelson, 2007). These figures illustrate one reason why adolescence is a period of special vulnerability for the later development of an SUD.

Unfortunately, the brain of the child or adolescent is also 4–5 times more vulnerable to alcohol-induced brain damage as is the brain of an adult alcohol abuser (Tapert, Caldwell & Burke, 2004/2005; Wuethrich, 2001). During adolescence, the **hippocampus**²⁰ appears to be especially vulnerable to

¹⁴Taking one puff off of a marijuana cigarette once a month, as opposed to smoking an entire marijuana cigarette each day, for example.

¹⁵A process called "synaptic pruning" by neurologists.

¹⁶See Glossary.

¹⁷See Glossary.

¹⁸See Glossary.

¹⁹As any parent of a teen age could tell you.

²⁰See Glossary.

alcohol-related damage (De Bellis et al., 2000; Tapert et al., 2004/2005). This might account for the small (7–10%) but still significant decline in psychological test performance in adolescent alcohol users as compared with nondrinkers (Strauch, 2003). This decline in measured cognitive abilities appears to be enhanced by concurrent use of marijuana, and could be permanent (Spear, 2010; Wagner, 2009). In theory, this reduction in cognitive abilities might reflect alcohol-induced damage to the hippocampus, and possibly other regions of the brain.

The “Gateway” Theory

This controversial theory was espoused by Henry Anslinger, then the U.S. Commissioner of Narcotics, to justify making marijuana illegal after the end of Prohibition, thus providing a rationale for the continued existence of the Bureau of Narcotics (McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds, 2009). Anslinger provided Congress with lurid tales of depraved behavior by marijuana users, many of which were fabrications, to justify making marijuana illegal. As part of this campaign, Anslinger also proposed (with remarkably little evidence) that marijuana use would prove to be a “gateway” to the use of more serious compounds. Since then, the gateway theory has become part of clinical lore (McPherson et al., 2009).

This theory has generated controversy for more than 70 years now. The team of Walker, Venner, Hill, Myers, and Miller (2004) found that there appeared to be a progression in adolescent substance use starting with alcohol, leading to tobacco, then the inhalants, marijuana, and then other drugs of misuse. In another test of the gateway theory, the team of Ellgren, Spano, and Hurd (2006) administered cannabis to adolescent rats, and then offered the rats the opportunity to use heroin. The authors found that the marijuana-exposed rats were more likely to self-administer heroin than were marijuana-naïve rats. The authors interpreted this as evidence for the gateway theory.

In contrast to this conclusion, Rosenbloom (2005) suggested that the gateway theory is just an illusion and that the progression from one compound to another is not automatic. Several groups of researchers have concluded that personality characteristics such as risk-taking, tobacco use, and a conduct disorder in childhood or adolescence might be more predictive of subsequent substance use disorders than simple marijuana use in adolescence (Clark, Vanyukov, & Cornelius, 2002; Marshall, 2014; Watson, Benson, & Joy, 2000). More doubt on the gateway theory was generated by the study conducted by Tarter, Vanyukov, Kirisci, Reynolds, and Clark (2006). The authors reported that about 25% of the 200 male participants who admitted to the use of marijuana did

use this compound *before* using alcohol or tobacco products, but that the majority of those who used marijuana did not progress to the use of other drugs.

Another challenge to the gateway theory of substance use came from Kandel and Chen (2000), who examined the marijuana use patterns of a community-based sample of 708 individuals who used marijuana (364 male and 304 female), and found that the early use of marijuana was not found to predict later problems with chemicals or a progression to later substance use (Kandel & Chen, 2000). This study was supported in part by the study conducted by Perkonig and colleagues (2008). The authors followed a sample of 3,021 adolescents over a 10-year period, with interviews at 4 years and 10 years after the initial survey. The authors found that 7% of their sample reported that they had used cannabis only once, that 11% of their sample reported using it 2–4 times, and that only a minority of their sample (approximately 13%) met the criteria for a diagnosis of cannabis dependence at the start of their study, at the 4-year follow-up interview, and at the end of the study. They also concluded that those adolescents who reported five or more episodes of marijuana use were the most likely to continue to use marijuana during the early years of adulthood, but that the majority of their subjects did not continue to use marijuana. Surprisingly, there is little evidence suggesting higher levels of marijuana use in adolescents who live in states where marijuana can be prescribed for medicinal purposes (Hasin et al., 2015). However, the social milieu does appear to strongly influence adolescent marijuana use patterns, such that those states that are more tolerant of personal marijuana use appear to have higher levels of adolescent marijuana use than those states that are less tolerant (Hasin et al., 2015). Also, medicinal and personal use laws have only recently been enacted, and their long-term contribution to the adolescent marijuana use problem, if any, remains unknown.

One class of compounds that is frequently overlooked in the debate over the gateway theory of marijuana use are the inhalants. These compounds are often the first mood-altering chemicals that children or young adolescents experiment with (Hogan, 2000). For most children or adolescents, inhalant use is usually a transient phase, and so the individual’s risk for inhalant-induced brain damage is limited. Such abusers usually engage in episodic inhalant abuse for 1–2 years, after which time they gradually discontinue it. A very small minority of children or adolescents become long-term, possibly lifelong, users of inhalants, and an unknown percentage of children or adolescents who use inhalants go on to use other compounds. The role of inhalant use by these children or adolescents is open to debate: Were these individuals unwittingly ensnared by the effects of the inhalants and then turned to the use of other compounds, or were those

children or adolescents who used inhalants the most likely to develop other substance use disorders? At this point, there is no clear answer to these questions, and debate surrounding the very concept of the gateway theory of substance use disorders continues.

Tobacco Use by Children and Adolescents

Cigarettes and other tobacco products occupy a unique place in society: They are known to be addictive and destructive, yet they can be legally purchased by adults. In contrast to this, children and adolescents are forbidden by law to purchase or use tobacco products. In spite of the legal restrictions against child or adolescent tobacco use, an estimated 2,500 children try cigarettes each day (Center for Behavioral Health Statistics and Quality, 2016). The total number of adolescents who smoke cigarettes has been slowly declining since 1991, and the percentage of twelfth-graders who reported ever smoking a cigarette from 2006 to 2016, as opposed to having smoked in the past 30 days, is reviewed in Figure 20-3 (based on Johnston et al., 2017).

This data reveals two different trends: First, there has been a downward trend for adolescent cigarette smoking in the United States over the past decade. The data suggests that perhaps half of adolescents who have tried cigarettes are apparently not addicted to tobacco, since they were able to abstain from smoking entirely for the past 30 days, according to Johnston and colleagues (2017). Arguably, this data might be interpreted as supporting the hypothesis that a large percentage of reported adolescent smoking reflects experimental cigarette use rather than addiction. Still, each day in the United States approximately 400 children or adolescents become daily cigarette smokers (Center for Behavioral

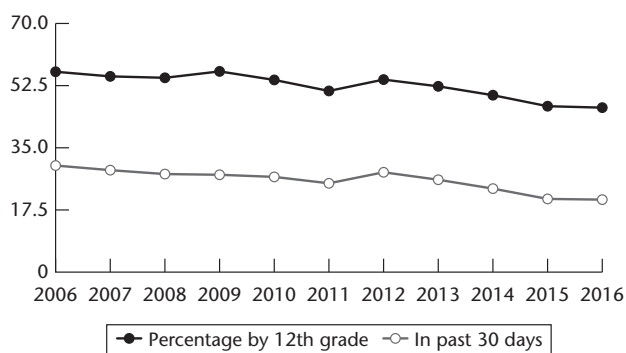


FIGURE 20-3 Percentage of High School Seniors Reporting Having Smoked.

Health Statistics and Quality, 2016). It is not known what percentage of these adolescents are or will become addicted to tobacco products, although this is a very real danger for those who even experiment with cigarette smoking.

A small percentage of adolescents (about 5%) use “smokeless” tobacco. When asked, many adolescents will offer the explanation that this is a safer method of tobacco use, that they are attempting to quit, etc. However, the team of Agalu, Ayo-Yusuf, Vardavas, Alpert, and Connolly (2013) found that rather than replacing the adolescent’s cigarette smoking, the use of chewing tobacco *supplemented* it, possibly allowing the user access to nicotine in situations where smoking was prohibited, such as a student in class, for example. Approximately 46% of adolescents have experimented with tobacco smoking through the use of a water pipe, as opposed to the 25% of adolescents who have experimented through regular cigarette smoking (Zahlan, Ghandour, Yassin, Affin, & Martins, 2014). The health risks associated with smoking tobacco through a water pipe have not been fully explored; however, the authors found that adolescents who smoked tobacco with a water pipe were also significantly more likely to engage in prescription drug misuse, suggesting that those adolescents who engage in this practice might be a distinct subpopulation of adolescents who experiment with tobacco use.

There is a growing trend for adolescents to experiment with electronic, or “e-cigarettes”²¹ and to be more accepting of this practice by peers. Increasingly strict controls seeking to limit access to e-cigarettes by adolescents appears to be forcing those adolescents who wish to access nicotine to turn to traditional cigarettes (Friedman, 2015). Unfortunately, most adolescents do not understand the addictive potential of nicotine or the destructive power of many of the compounds found in cigarette smoke. The only assured way to avoid the possibility of addiction to nicotine, the primary addictive ingredient in cigarettes, is never to smoke. If an adolescent does begin to smoke and becomes addicted to nicotine, there are at best only limited resources to help that individual quit (Blum, 2006). What might be termed “Big Tobacco” most certainly has an investment in reinforcing the incentive to smoke among children and adolescents. One major tobacco company has conducted research into the phases of cigarette smoking in adolescents (Hilts, 1996), while another tobacco company referred to adolescents in an internal memo as an “up and coming new generation of smokers” (Phelps, 1996, p. 1A). The R.J. Reynolds Tobacco Company, most certainly a major cigarette producer, went so far as to refer to 12-year-olds as a “younger adult” generation of smokers (“Big Tobacco’s secret kiddie campaign,” 1991).

²¹ The use of e-cigarettes is also called “vaping” in some areas.

The neurological and behavioral immaturity of adolescents will make it difficult for them to accurately assess the risks associated with various behaviors, including cigarette smoking (Pumariega & Kilgus, 2005; Strauch, 2003). Indeed, there is evidence that for adolescents who smoke to help build their self-esteem, the warnings on the side of cigarette packages serve as an enticement to continue to smoke, to prove their courage (Hansen, Winzeler, & Topolinski, 2010). Thus, the traditional method(s) of providing adolescents with information about the dangers of cigarette smoking might prove to have the opposite effect.

The tobacco industry spends \$9.1 billion a year to advertise its products (U.S. Federal Trade Commission, 2016), usually in a format likely to be accepted by adolescents. Having peers who smoked cigarettes was an even stronger influence on individual smoking behavior than exposure to advertising (Hansen et al., 2010). Another influence on adolescent smoking behavior is whether the individual's parents smoke. This is supported by the observation that the majority of adolescents who smoke have parents who also smoke cigarettes.

Stages of Childhood/Adolescent Smoking

The child or adolescent's transition from a nonsmoker to active cigarette smoking passes through four phases (Holland & Fitzsimons, 1991): (1) the *preparatory phase*, during which time the individual forms attitudes accepting of cigarette smoking; (2) the *initiation phase*, when the individual smokes for the first time; (3) the *experimentation phase*, when the smoker learns how to smoke after the first tentative smoking efforts; and (4) the *transition phase* to regular smoking. It is thought that proper intervention during any of these stages will reduce the chances that the individual will develop a long-term tobacco use disorder.

Why Do Children and Adolescents Use Chemicals?

Substance use disorders in childhood and adolescence do not arise in isolation, but are influenced by the individual's (a) constitutional predisposition (genetic heritage), (b) environmental factors (lack of parental supervision, exposure to parents who misuse substance, peer groups, neighborhood,²² etc.), and (c) life events (child abuse, victimization,

etc.) (Levi, Segal, De Beasi, & Martin, 2015; Upadhyaya & Gray, 2009). Further, there are the ongoing processes of physical, emotional, and neurological development during childhood and adolescence. Children, and most certainly adolescents, normally are becoming more independent, and as any parent will attest, they are more than willing to tell you that they do not need to be told what to do! Unfortunately, a consequence of the process of neurological maturation for children and adolescents is that the individual is unable to adequately assess inherent risks in behaviors such as substance use, because those regions of the brain responsible for this task do not fully mature until young adulthood. As a result of this developmental delay, children and adolescents tend to underestimate the negative consequences of high-risk behaviors, occasionally with dire results (Dobbs, 2011; Hogan, 2000; Pumariega & Kilgus, 2005). This is supported by the observation that risky alcohol use behaviors peak in the 16–20 age cohort, and rapidly declines in frequency after that age (Chartier, Hesselbrock, & Hesselbrock, 2010).

Hogan (2000) offered five basic reasons why children and adolescents use chemicals (Hogan, 2000; Millar, 2009): (1) to feel grown up, (2) to take risks or rebel against authority, (3) to fit into a specific peer group, (4) to relax and feel good, and (5) to satisfy curiosity about the effects of that compound(s). Drawing upon their survey data, the team of Johnston et al. (2012a) suggested that the majority of those who admitted to ever using an illicit substance did so on an experimental basis and did not use that compound more than a few times, supporting the "curiosity" hypothesis.

As noted above, children and adolescents often engage in alcohol use because it helps make them feel older. This might also account for the growing trend for older children and adolescents to use narcotic analgesics that they find in the medicine cabinet of the family or friends' homes. Unfortunately, they do not understand the risk of an overdose due to their small body size, as contrasted to the medication dose, which is usually calculated for an adult. Some adolescents view various chemicals as an acceptable way to self-medicate negative feelings such as depression or perceived levels of stress (Spear, 2010; Wills, Sandy, Yaeger, Cleary, & Shinar, 2001), or to demonstrate sexual prowess (Barr, 1999). As this list indicates, there is really no simple answer to why children and adolescents use chemicals. There are also other factors that will influence childhood and adolescent substance use patterns, which will be discussed below.

Racial/Ethnic Group Membership

The research team of Johnston and colleagues (2017) found that African American adolescents have reported significantly lower rates of alcohol and drug use than Hispanic or

²² Is the child growing up in an impoverished, lower-, middle-, or upper-class neighborhood?

Caucasian children, but these differences are shrinking due to greater use of marijuana in African American adolescents. This is consistent with the observation that substance use disorders are most commonly found in Caucasian, middle-class adolescents. These are the individuals who are most likely to have money for discretionary spending, and possibly experience lower levels of parental supervision because both parents have to work to maintain their established lifestyle.

The ethnic heritage of the adolescent has been found to influence that individual's substance use behaviors (Shih et al., 2010). Asian American children were less likely to smoke cigarettes or use alcohol, for example, especially if they perceived that such behaviors were unacceptable to siblings or to parents. Hispanic students frequently lack the "life skills" to reject offers of substance use, the authors found, while Caucasian students might view substance use as a way to become more popular. Educators needed to focus on the appropriate intervention for the ethnic composition of the student population rather than apply a generic approach to the task of teaching students about drug use, according to the authors.

Gender Differences

Adolescent males have been more likely to use illicit drugs by a factor of 2:1 as opposed to adolescent females by the time of high school graduation (Johnston et al., 2012a), but this gap has been closing in recent years (Johnston et al., 2017). Males are generally more likely to be heavy users of illicit drugs than are adolescent females, according to the authors. One exception to this is the use of amphetamine compounds, which seem to be most commonly used by adolescent girls, a difference that is possibly motivated by a desire for weight loss/control purposes by the adolescent girls in their sample. Finally, the authors noted that the observed difference in prevalence rates between male and female adolescents appears in middle to late adolescence, which other research has demonstrated is when adolescent males are most likely to engage in impulsive, risky behavior.

Parental–Adolescent Relationship Patterns

Parents often forget that children (and adolescents) learn by interacting with and observing their parents, especially the behavior of the same-sex parent (Patock-Peckham & Morgan-Lopez, 2006). Later, they also begin to observe other adults and their peers, as they begin a lifelong process of social observation and learning. These early learning experiences are so important that research suggests that the pattern of parental interactions, especially how they resolve conflict, might affect the child's mental health as much as

30 years later ("Deteriorating home life puts kids at risk," 2009). Unfortunately, parents often dismiss their influence on the developing child or adolescent, especially during the latter period of life, when in reality they still retain strong influence on fundamental issues such as behavioral morality, religion, and the perceived importance of education for their adolescent children (Windle et al., 2009).

Although many parents believe the contrary, parent–child relationship influences are generally stronger than those of adolescent peer groups, especially when the parents monitor their child's peer group membership. It is within the context of the parent–child relationship that children begin the social learning process referenced in the last paragraph, internalizing lessons provided by the parents, siblings, and parental substitutes²³ through passive observation. Watching an older sibling being punished for unacceptable behavior (such as throwing something across the room in anger, for example) offers the child the opportunity to engage in the process of passive learning. If the child should emulate their older sibling and meet a similar punishment, he or she starts the process of active learning. In this manner, behavioral rules are transmitted to the young child, playing a role in future behavioral choices (Hill, Steinhauer, Locke-Wellman, & Ulrich, 2009).

Consider, if you will, two hypothetical families on the day after Thanksgiving. In one family, the maternal uncle became grossly intoxicated during Thanksgiving dinner and started a fight with the child's father. The next day, when the 3-year-old son inquires why his uncle became so angry and aggressive the day before, his mother simply replies, "Oh, that's the way that your uncle is when he drinks too much." In the second family, a maternal uncle also becomes grossly intoxicated and starts a fight with the child's father. The next day, when the 3-year-old son inquires why his uncle became so angry and aggressive, his mother replies, "That was disgusting behavior on your uncle's part. He drank far too much and embarrassed everybody by his behavior! It was sickening! I don't ever want to see you act that way!"

Children often learn about the negative effects of alcohol and parental attitudes toward other forms of drug use through passive observation (Donovan, Molina, & Kelly, 2009; Thatcher & Clark, 2008). The quality of parental supervision, openness to communication between the parent and the child, and enforcement of parental rules also play roles in helping the child and adolescent develop expectations for recreational substances. It is within the context of the family that behavioral decisions including substance use initiation

²³ Such as a respected teacher, to cite one example among many.

are made by the adolescent (Winters, Botzet, Fahnhopst, Arria, Dykstra, & Oliver, 2012). Further, in spite of parental beliefs to the contrary, parents still retain a strong influence on fundamental issues such as morality, religion, and the perceived importance of education in adolescents (Windle et al., 2009).

A major factor that influences adolescent substance use patterns is parental *control* or supervision (Griffin & Botvin, 2010; Levi et al., 2015; Patock-Peckham & Morgan-Lopez, 2006; Windle & Zucker, 2010). Although many parents view themselves as powerless by the time their child reaches adolescence, in reality they retain a large degree of leverage over the adolescent's (a) cash flow, (b) credit card use, (c) access to a car, (d) curfew, (e) cell phone use and access, and (f) computer use and access. In many states, adolescents under a designated age must have parental consent to hold a part-time job, which provides another element of leverage for the parent. Adolescents who report the highest levels of parental monitoring²⁴ and enforcement of rules have lower levels of misconduct, delinquency, and substance use²⁵ (Bahr & Hoffmann, 2010; Kaminer, 2008; Levi et al., 2015; Patock-Peckham & Morgan-Lopez, 2006; Tildesley & Andrews, 2008). This degree of parental supervision allows for intervention should the adolescent start to stray into dangerous territory, although such punishment should not be harsh or excessive²⁶ (Griffin & Botvin, 2010). The parent also retains some degree of control over the people the adolescent associates with, although this power is not as strong as it was during the individual's childhood. These can provide powerful tools for parents attempting to control or modify unacceptable behaviors, including substance use, by their child or adolescent.

A factor that reflects the continued presence of parental influence during adolescence is the child's ability to *communicate* with the parents, to ask questions and express concerns about their exposure to individuals who use alcohol or drugs. Not surprisingly, there is evidence that adolescents who associated with friends whose parents were warm and open to

communications, but who also set and enforced limits were themselves less likely to engage in behaviors such as cigarette smoking or alcohol use (Shakya, Christakis, & Fowler, 2012).

The social learning process that begins in childhood and continues through adolescence is a two-edged sword: There is a strong relationship between *parental* substance use patterns during the childhood years, and subsequent substance use behavior of the adolescent (Brown et al., 2009; Chassin, Flora, & King, 2004; Donovan et al., 2009; Griffin & Botvin, 2010). By the age of 17, 51% of adolescents will have seen one or both parents intoxicated on at least one occasion (National Center on Addiction and Substance Abuse at Columbia University [CASA], 2009b). Two percent of women with children²⁷ living at home meet diagnostic criteria for an illicit drug use or medication use disorder (Simmons, Havens, Whiting, Holz, & Bada, 2009). The experience of viewing parental intoxication in the face of parental admonitions against drinking or illicit substance use provides conflictual information to the child or adolescent²⁸ (CASA, 2009b; Donovan et al., 2009), and this might be one reason why children whose parents have an alcohol use disorder also tend to have higher rates of alcohol abuse and an earlier onset of social medical problems later in life (Tildesley & Andrews, 2008).

One frequently overlooked element of the child's relationship with his or her parents is the quality of the *attachment bonds* that develop with the parents in childhood (Bell, Forthun, & Sun, 2000; Flores, 2004; Hogan, 2000). Children with positive attachment bonds tend to be resistant to the urge to engage in substance use, have more positive peer relationships, are more socially competent, and demonstrate better coping skills than adolescents who have a more troubled relationship with their parents. Such strong attachment bonds are expressed by such parental behaviors as consistently spending time with their children, positive parental substance use modeling behavior, and the degree of parental emotional involvement in the lives of their children (Kaminer & Buckstein, 2005).

Parents, especially those with poor communication bonds with their children, tend to underestimate the level of substance use by their child or adolescent: One percent of parents expressed the belief that their child had used a CNS stimulant to help them study, for example, whereas 10% of high school seniors say they have engaged in this practice ("By the numbers," 2013). They are less aware of

²⁴Such as parental monitoring of (a) who their child is with, (b) where the child is, (c) the child's report of their activities and its congruence with feedback from other adults, (d) when the child will return, and (e) whether they actually do the things they tell the parents they want to do.

²⁵This is not to say that strict parental rules will *prevent* adolescent substance abuse. But high levels of parental monitoring and enforcement of established rules are generally associated with lower levels of deviant behavior(s), including alcohol or illicit drug abuse.

²⁶In contrast to situations where the parent belatedly starts to assert parental authority. A sudden attempt by the parent to assert such authority will likely be met with levels of resentment and resistance far beyond that seen in healthy parent-child relationships. As the battle for control rages, many inadequate parents will retreat, leaving the adolescent to set their own boundaries.

²⁷Defined as under the age of 18 years.

²⁸"Don't do as I do, but do as I say!" A behavioral stance that adolescents are quick to dismiss as parental hypocrisy.

issues such as adolescent marijuana use, as evidenced by the observation that 80% of parents expressed the belief that recreational chemicals were not at parties their children attended, whereas 50% of adolescents reported that both alcohol and drugs were freely available at these parties (Sheff, Warren, Ketcham, & Eban, 2007). Drawing on a sample of 432 adolescents and at least one of their parents, Delaney-Black and colleagues (2010) found that parents were eight times as likely to under-report personal use of cocaine and opiates when asked, while adolescents were 52 times as likely to do so. This study illustrates how parental modeling behaviors help to shape the adolescent's substance use, but also how often adolescents deny the use of drugs even in the face of evidence to the contrary.

As a group, parents underestimated teenaged alcohol consumption by a factor of 4:1, inhalant use by a factor of 4:1, and illicit drug use by a factor of at least 2:1 (Center for Substance Abuse Research, 2006). However, this lack of parental awareness appears to be strongest during early adolescence, perhaps reflecting parental awareness of the possibility of substance use by middle- and late-stage adolescents (McGillicuddy, Rychtarik, Morsheimer, & Burke-Storer, 2007). Parents who struggle with psychosocial adjustment issues of their own are also less likely to be aware of their child's substance use pattern, according to the authors.

Siblings

Feedback from siblings is an important, but rarely studied, component of the substance use disorders in adolescents (Griffin & Botvin, 2010). An older sibling who is a drug user might set a negative example for a younger brother, or an older sister's feedback might discourage her younger sister from initiating alcohol use in early adolescence, for example. However, as noted, this area has not been explored in detail, and there is much to learn about the role feedback from siblings plays in the development of or resilience against subsequent substance use behaviors.

Vocational/Occupational Choices

There is strong evidence of an association²⁹ between time spent working and tobacco or alcohol use by adolescents in school. Those students who spent more time at work than they did on study were more likely to engage in alcohol and tobacco use (Wagner, 2009). They were also more likely to seek part-time jobs consistent with their vocational interests,

and to spend more time working on a part-time basis than their more academically minded counterparts (Mortimer, 2010). The individual's initial occupational choice following graduation also is associated with substance use behaviors. Adolescents who enlist in the military, for example, sever traditional sources of support such as peers and parents, while simultaneously entering a subculture in which heavy alcohol use is accepted (Ames, Duke, Moore, & Cunradi, 2009; Benton, 2009; Zucker et al., 2009). In both the military and other occupations, heavy drinking subgroups develop that provide a sense of belonging (Benton, 2009). It is within these subcultures that the adolescent completes the transition from adolescence into the first stages of adulthood. Behavioral choices made during this transitional period often are continued into adulthood.

Adolescent Mood States

It is rather simplistic to say "negative feelings" can contribute to the impulse to use alcohol or illicit chemicals. What is a "negative feeling"? Are there universal negative feelings, or does each person rate the intensity of their feelings differently? How intense does a feeling of depression have to become, for example, before it can be classified as a negative feeling as opposed to a normal mood swing? If a given adolescent who suffers from a major depression should also be using alcohol or illicit drugs, does this imply a causal relationship? There is mixed evidence, for example, suggesting that disorders of affect in adolescence might play a role in the development of an SUD in this age group (Rutherford et al., 2010). The authors suggested that disorders of emotional control increase the risk for the subsequent development of an SUD for girls, but that behavioral dyscontrol problems appear to be of greater importance for the development of an SUD in boys. Thus, the issue of the gender-specific impact of negative mood states is raised: Are boys affected the same way as girls by a specific negative feeling?

Depression and other mental health struggles are frequently identified as risk factors for adolescent substance use (Kaminer, 2008; Kriechbaum & Zernig, 2000; Roten & Gray, 2015). Unfortunately, the correlation between depression and SUDs is a modest one at best, and is stronger for girls as opposed to boys (Fleming, Mason, Mazza, Abbott, & Catalano, 2008). The authors found that depression in early adolescence was positively correlated with alcohol, marijuana, and cigarette use for adolescent girls, but only for marijuana use for boys. This might reflect the fact that few adolescent boys, like their adult counterparts, recognize the existence of their depression or other negative emotional states (Mayeda & Sanders, 2007). Adolescent girls tend to be more in touch with feelings such as depression or anxiety, and it is for this reason that the impact

²⁹ As before, associational relationships are not the same as causal relationships.

of affective disorders on substance use behaviors differs between adolescent boys and girls.

One interesting study was conducted by Rao, Hammen, and Poland (2009). The authors measured the **cortisol**³⁰ levels in 151 adolescents (a process that required the collection of urine for 24 hours from each individual for testing). The authors found that adolescents who had higher levels of cortisol in their urine (an indication of stress, often a precipitant of depression in adolescents) were more vulnerable to the development of substance use disorders. Where an adult might require 2–7 years of habitual substance abuse before he or she becomes addicted to that substance, adolescents might become addicted to the same compound in as little as 12–18 months (Freimuth, 2005). The results of this study lend support to understanding the relationship between depression and subsequent SUDs in adolescents.

It is often surprising for parents to learn that behavioral extremes may signal problems for the adolescent (Lundeen, 2002). Total abstinence from any substance use during adolescence has been identified as a signal of possible impending problems. The critical issue is not whether the adolescent uses alcohol or illicit drugs so much as *which compounds, how often, and in what quantities*. The adolescent who frequently uses alcohol or drugs tends to have poor impulse control, be socially alienated, and experience high levels of emotional distress, all warning signs that the individual may lack the social skills necessary to cope effectively. In contrast, the adolescent who is totally abstinent from alcohol and illicit drugs may be anxious, emotionally constricted, lack self-confidence, and may lack the social skills necessary to cope with life's demands. Thus, the adolescent's substance use pattern must be viewed within the context of his or her emotional adjustment.

Conduct Disorder/Oppositional Defiant Disorder

There is a known relationship between behavioral control disorders in childhood and the subsequent development of substance use disorders. Both of these disorders share the common traits of impulsiveness and limited behavioral control, increasing the individual's risk for the development of an SUD (Clark et al., 2002). Behavioral problems usually precede the development of adolescent SUDs, possibly reflecting a common neurological basis for these conditions (Clark et al., 2002; Newcorn & Ivanov, 2007). Further, some have found that children with difficult temperament may develop conduct disorder (CD) or oppositional defiant disorder

(ODD) (Bukstein & Kaminer, 2015). It is estimated that 50–80% of adolescents with a diagnosis of CD will develop a substance use disorder at some point in their lives (Kaminer & Buckstein, 2005). However, the relationship between impulsiveness and substance use is not entirely clear, and for some adolescents substance use might *precede* impulsive behavior(s) (Rutherford et al., 2010). There is thus a need for further research to determine the exact relationship between impulsiveness and substance use in adolescence.

The prefrontal cortex of the brain is actively involved in the process of assessing potential risks and behavioral control. Preliminary evidence suggests that individuals with CD and ODD, as well as adults with antisocial personality disorder, have altered neurological function in this region of the brain, possibly contributing to the behavioral problems central to either disorder. In order for a rehabilitation program to be effective, it is necessary to develop a program that addresses the issues of behavioral control into the SUD rehabilitation program (Clark et al., 2002). Such programs should not, however, be based on describing the negative consequences of substance use, as adolescents often view substance use in the face of these warnings as an expression of willingness to take risks and thus of gaining social status.

Peer Group Influences

Parents often overestimate the influence of peer groups on the behavior of their child or adolescent. Research findings suggest that peer groups *do* influence the individual's behavioral decisions; however, peer group influence peaks between the ages of 11 and 13 (Cleveland, Feinberg, & Jones, 2012). In a manner that parallels the neurological maturation process, the adolescent's substance abuse in late adolescence is more frequently a *planned* activity and less likely to be in response to social opportunities to engage in substance use (Cleveland et al., 2012). Adolescent abstinence from alcohol or illicit chemicals is also more likely to be a planned behavior rather than a response to external constraints (Cleveland et al., 2012). Peer group influences are not always negative: Peer approval (or disapproval) might prove to be more important to the individual than the pharmacological reward potential of a compound that might be used. In this case, the behavioral choices encouraged by the adolescent's peer groups may serve as either a protective or a negative influence on adolescent substance use behaviors (Brook, Pahl, & Rubenstone, 2008; Chartier et al., 2010; Ross, 2002; Simkin, 2002).

The results of peer association studies must be interpreted with some degree of caution, because the individual chooses his or her peers. Further, peer group membership is not automatically mutually exclusive: Any individual might

³⁰ See Glossary.

associate with members of different peer groups should they wish to do so. However, peer influences are important determinants of the marijuana use patterns of the adolescent (Mir, Amialchuk, & Dwyer, 2011). The study of adolescent obesity carried out by the team of Gessel, Tesdahl, and Ruchman (2012) provided partial support for this hypothesis: The authors concluded that those children and adolescents who associated with physically active peers were themselves more likely to be physically active. However, there is a self-selection process through which adolescents who are unwilling to be physically active drift away from their more active peers toward those who are less physically active.

The role of peers in substance use disorders is also limited by the pharmacology of the substance being used. Peers might strongly influence the *initiation* of substance use, but their role in supporting its continued use is not as important as the pharmacological reward potential of the compound(s) being used. As a result of this process, adolescents tend to gravitate toward peer groups with views of substance use, values, expectations, and behavioral demands similar to their own (Mir et al., 2001; Pumariega & Kilgus, 2005; Simkin, 2002; Valente, Gallaheer, & Mouttapa, 2004). This gravitational process would suggest that peer group selection is the *last* step in the chain of events that results in the adolescent joining a subgroup in which substance use is tolerated if not encouraged.

Telecommunications

The adolescent peer group affiliation is compounded by the telecommunications era.³¹ The development of personal telecommunications devices such as the cell phone, which allows for much more than phone conversations, such as text messaging, snapchatting, and a variety of other apps, allows the adolescent to maintain a tenuous “relationship” with persons they might never meet in person. The average teen may send hundreds of messages a day, often sending comments and photos they would never share in person. These electronic adolescent interactions can be carried out from a distance, often in a clandestine manner that potentially circumvents parental supervision.³² The telecommunications era is still evolving; however, it is clearly a potential contributing factor to unhealthy adolescent behaviors.

³¹ This is especially true in the current era of telecommunications: Any individual might exchange text messages, photos, or e-mail messages with members of a wide range of social groups.

³² How many parents *really* take time to check to see who their teen has been sending messages to, or receiving messages from on a consistent basis?

Religious Affiliation

A recent study by Muschel, Ratner-Stauber, Mardolis, Demaria, and Schechter (2013) spans both the influence of the individual's involvement with religious activities and the family. Surprisingly, affiliation with and participation in religious activities in childhood appears to influence alcohol use patterns throughout adolescence and into adulthood. Those individuals who were members of more structured faiths that provided a firm identity³³ and that had an established moral code were able to use these resources to help them delay the initiation of alcohol use in adolescence (Koenig, Haber, & Jacob, 2011; Latimer & Zur, 2010). African American youth are more likely to be religious than their Caucasian peers, possibly because religion plays such a large role in African American culture, which would seem to explain why this subpopulation is less likely to engage in alcohol use as children and adolescents (Vaughan, de Dios, Steinfeldt, & Kratz, 2011). Thus, there is an emerging body of evidence suggesting that membership in a structured religion in childhood and adolescence reduces the odds that the individual will engage in alcohol use during these periods of life (Mason & Spoth, 2011).

Music Selection

The typical adolescent spends approximately 2 hours each day listening to music. The team of Primack, Dalton, Carroll, Agerwal, and Fine (2008) examined the content of the music that adolescents listen to, and found either implicit or explicit references to substance use in a significant percentage of songs examined. The authors found that alcohol was the most commonly referenced substance, followed by marijuana. They also found that rap music contained the greatest percentage of references to substance abuse (more than three-quarters of songs sampled), while pop music had the least (10% of songs sampled). This disturbing finding is made even more frightening by the content of the references to alcohol or substance use, which usually glorified the use of the compounds in the content of the song, associating the use of these compounds with sexual, emotional, and/or financial gains for the user (Miller, 2008). It is not clear at this time whether the adolescent's choice of music is a response to his or her use of chemicals, is just a phase through which the adolescent must pass,³⁴ or whether the individual is predestined to use alcohol or drugs, but it has been determined that

³³ Such as the Catholic Church, more conservative Jewish denominations, etc.

³⁴ In the sense that the adolescent finds such music exciting for a period of time, and then discards this form of entertainment in favor of another form of music.

music can have a negative effect on the individual's efforts to recover from chemical use disorders (Short & Dingle, 2015). However, these findings are disturbing.

Personal Values

An often overlooked aspect of substance use disorders are the individual's values, which reflect their emerging personality. The child's parents help to establish the personal values that will grow over time. These may carry out a protective function protecting against or facilitating the development of adolescent substance use disorders, depending on the individual's values. There is a negative correlation between substance use and such factors as (van den Bree & Pickworth, 2005) academic achievement, church attendance, the individual's beliefs about the importance of academic achievement, and participation in organized sports (Latimer & Zur, 2010; Levi et al., 2015). However, it is not clear whether these factors help to protect the adolescent from SUDs or not, since correlation does not imply causality.

Rebellion

A factor that is closely intertwined with personal values is the adolescent's attempts to rebel against perceived parental authority. The natural rebelliousness of adolescents makes them vulnerable to the image of cigarette smoking as a way to rebel against parental authority (Dickinson, 2000; Greydanus & Patel, 2005), for example. This image is encouraged by tobacco companies, especially through advertising. Morgenstern, Sargent, Isensee, and Hanewinkel (2013) found, for example, that for every 10 cigarette advertisements seen by the adolescent, the risk that the individual would take up smoking went up 38%. The use of other chemicals also appears to many adolescents to be an avenue through which they can express their rebellion and independence (Griffin & Botvin, 2010). However, there is a difference between isolated acts of rebellion and delinquency or conduct disorders. Periods of heavy drug use appear to serve as a catalyst for subsequent criminal activity in some groups (Heyman, 2009). Parental authority appears to hold such acts of rebellion in check, or at least limits their expression, while the lack of appropriate parental authority encourages the development of the latter problems.

Insomnia

An interesting theory was introduced, suggesting that those adolescents who suffer from insomnia are at higher risk for later depression and SUDs ("Adolescents with insomnia are at risk for future substance abuse and depression," 2008). The average adolescent requires between 8.5–9.25 hours of sleep

per night, although at first their sleep pattern shifts to one where they go to sleep later and wake up later than do their older peers (Brown et al., 2009). Adolescents who sleep for shorter periods force sleep deprivation states on themselves in spite of "catch-up" opportunities for extra sleep on the weekends (Brown et al., 2009).

Although one might expect that sleep deprivation would be the result of substance use, an emerging body of evidence suggests just the opposite: Adolescents who habitually are sleep-deprived may learn their sleep habits from friends, with the greater the number of sleep-deprived friends being positively correlated with cannabis use by the adolescent (Roane & Taylor, 2008; "Social networks show drug use . . .," 2010). Further, a surprising problem, once thought to be seen only in adults, is the possibility that the adolescent might suffer from **obstructive sleep apnea**,³⁵ a medical condition that causes sleep disruption and that appears to raise the adolescent's risk for an SUD, in part through its ability to induce depression.

Abuse History or Victimization

There is a body of evidence suggesting that physical, sexual, and emotional abuse during childhood and adolescence might be associated with the development of SUDs later in life (Clay, Allen, & Parran, 2008; Oshri, Rogoscu, Burnette, & Ciccette, 2011). Thirty to sixty percent of women in primary substance rehabilitation report having experienced such severe levels of abuse that they meet the diagnostic criteria for posttraumatic stress disorder (PTSD). While the exact causal mechanisms for this association have yet to be identified, it is thought that severe abuse could cause a dysregulation of the normal stress-response mechanisms in the body, which in turn could block normal maturation of the brain in adolescence and early adulthood, especially in the frontal and prefrontal cortex, the regions that govern behavior and anticipate the consequences of behavior. More research is necessary to confirm whether this theory is accurate, but it does seem to be a mechanism through which physical, emotional, and sexual abuse might be associated with later SUDs.

Employment

Research has demonstrated that many persons begin to work on an informal basis (mowing lawns, babysitting, etc.) at around the age of 12 years, although by the age of 16 years the individual is more likely to have graduated to a more formal part-time job (Mortimer, 2010). Part-time employment

³⁵ See Glossary.

during adolescence provides the individual with a source of income that might be used for various items deemed important by the adolescent, including alcohol and drugs (Mortimer, 2010).

Section Summary

It is tempting to blame a single factor such as peer group influence for child or adolescent substance use. In reality, such a belief is too simplistic: Identified risk and protective factors in childhood or adolescence are not destiny. At most they hint at the possibility that the child or adolescent *might* develop a substance use disorder later in life (Winters et al., 2012). Unfortunately, adolescent substance use takes place during a period of social and neurological vulnerability, and the adolescent brain appears to be hard-wired to put emphasis on environmental experiences that bring pleasure. This, plus the still evolving frontal regions of the brain, combined with lax parental supervision and a permissive social environment, are forces that help increase the individual's risk for developing a substance use disorder in adulthood (Fiellin, 2008).

Substance Use: How Much and When Does It Become Too Much?

Prevention

Treatment of adolescent substance use disorders is often difficult to arrange, and its efficacy lacks research support. Ultimately, modifications to these early intervention programs are probably going to be necessary to make them more effective. However, society has finally started to recognize that *preventing* the development of substance use disorders in children and adolescents is more cost-effective than treatment after the disorder develops. Griffin and Botvin (2010) suggested that these early prevention programs might fall into one of three categories: (a) universal, (b) selective, and (c) targeted. Universal-level prevention programs focus on the population of the age cohort for which the program is designed, with the goal of delaying or preventing the onset of substance use. Thus far, research indicates that these programs may be best for those who are at low risk (Bukstein & Kaminer, 2015). Selective prevention programs focus on those children or adolescents who are at increased risk for the development of a substance use disorder because of environmental conditions or life circumstances. Targeted prevention programs are specifically aimed at those individuals who demonstrate the early warning signs of being vulnerable to the development of a substance use disorder. Lack of

evidence leaves those who are working in prevention wondering if universal prevention programs should be provided for all children or just focus on prevention for those who are at high risk (Bukstein & Kaminer, 2015).

Childhood

The issue of childhood substance use is both more clear, and more difficult, for clinicians. Substance use or misuse by children is usually hidden, and few parents or health care professionals ask the specific questions necessary to identify the problem. The dangers of experimental substance use by children are self-evident: Any use of alcohol or illicit compounds is potentially dangerous. The regular misuse of such compounds is certainly a sign of a serious problem. However, even if the child has been appropriately identified as having a substance use disorder, treatment resources for these children are virtually nonexistent (Millar, 2009).

It had been hypothesized that early onset alcohol use by children (defined as occurring before the age of 13) might reflect a genetic predisposition toward alcohol dependence (Agrawal et al., 2009). This conclusion is partially supported by the work of Hingson, Heeren, and Winter (2006), who found in their study of 43,000 adults in the United States that 47% of those who misuse alcohol began to drink before the age of 14, as opposed to just 9% of those who began to drink after the age of 21. Further, the younger the individual is at the time of drinking initiation, the more likely he or she will experience more severe alcoholism (Windle & Zucker, 2010). Similar information addressing the use of other chemicals is unavailable at this time.

Adolescents

Adolescence is a time of exploration as the individual continues the work of establishing a personal identity. Experimental substance use, especially of alcohol and marijuana, is potentially a part of this process of exploration. *Total* abstinence from alcohol and the drugs of misuse during adolescence is rare: Only 11% of adolescents abstain from all chemicals throughout adolescence (Chassin et al., 2004). By twelfth grade, half have tried at least one illicit drug (Johnston et al., 2017). For the majority of adolescents, *experimental* use of alcohol and marijuana appears to be the norm. Unfortunately, there are no firm boundaries between experimental use, substance misuse, and substance use disorders in adolescents. Experimental use is a risk factor for the development of a substance use disorder (Kaminer, 2008; Meyers & Dick, 2010); however, contrary to popular opinion, substance use in adolescence is not always a prelude to substance use disorder later in life (Heyman, 2009; Kaminer, 2008). Admittedly, some adolescents who misuse

substances do go on to become addicted to alcohol or drugs. The majority do not. This is supported by a study conducted by Knight and colleagues (2007), who found that while 44% of the 12- to 18-year-olds screened who were identified as having either a past or current history of alcohol or drug misuse, the majority of these individuals did not progress to substance dependence later in life.

Even experimental substance use places the parents of an adolescent in a dilemma: If they respond in a punitive, authoritarian manner, the individual might then continue substance use as an expression against parental authority. If the parents are too permissive in their response to their discovery of their child's³⁶ substance use, some adolescents will interpret this as tacit permission to continue to use chemicals. Parents who are concerned about their adolescent's substance use should consult a chemical dependency counselor who has the training to work with adolescents, or a child mental health professional with a clear understanding of substance use in children, to assist them in learning more effective parenting skills (Elkin, Fite, Moore, Lochman, & Wells, 2014).

Stages of Adolescent Substance Use

There are a number of paths that an adolescent might follow once she or he begins to use chemicals. Two examples are the models suggested by Greydanus and Patel (2005) and Parekh (2006). Each suggests that adolescent substance use proceeds through five stages, and the two models are contrasted in Table 20-1.

As has been stated before, the adolescent's progression from one stage to the next in either model is *not* automatic.

Social forces and the normal developmental process during adolescence can either facilitate or block the progression from one stage of substance use to another. For reasons that appear to reflect genetic vulnerability and social forces, progression of substance use appears to be both accelerated and is more intense for a small percentage of adolescents. In such cases, the time between entering Stage 0 and the start of Stage 4 on the Greydanus and Patel (2005) model can be a matter of just a few months following initiation of substance use (Greydanus & Patel, 2005; Rutherford et al., 2010).

Adolescent Addiction to Chemicals

The question of whether the adolescent substance user might become physically addicted to a compound has been quite controversial (Bukstein & Kaminer, 2015; Evans et al., 2005). This may be due in part to the struggle of labeling adolescents with an addiction, particularly when they may fit within typical norms for usage at their age, or are on the low end of the diagnostic spectrum (Bukstein & Kaminer, 2015). The diagnostic symptoms of SUDs normally found in adults who are dependent on a substance are not always found in the adolescent who uses substances (Evans & Sullivan, 2001; Pumariega & Kilgus, 2005). They rarely develop substance withdrawal syndromes seen in older patients (Johnson, 2012b),³⁷ and adolescents using substance rarely develop characteristic patterns of organ damage seen in adults addicted to chemicals. However, *tolerance* to the effects of their drug of choice can develop as rapidly (if not more rapidly) as in the adult using the same chemical(s) (Spear, 2010).

TABLE 20-1 Comparison of Two Models of Adolescent Substance Abuse

Parekh (2006)	Greydanus and Patel (2005)
(1) Initiation: First use of a mood-altering chemical (either alone or with peers.	Stage 0: No substance use, but is very interested in learning more about them, suffers low self-esteem, and is vulnerable to peer pressure.
(2) Learning the mood swing: Adolescent is taught (by experience or by others) what to look for in the use of a chemical(s).	Stage 1: Experimentation. No real negative consequences encountered yet.
(3) Regular use/seeking the mood: Continued use to maintain substance-induced pleasure.	Stage 2: Adolescent actively seeks drug's effects, centers life more and more around use of chemicals.
(4) Abuse/harmful consequences: Adolescent begins to encounter academic performance problems, etc., but continues to use chemicals.	Stage 3: Preoccupation with substance use by adolescent. Mood swings and acting out behaviors noted in this stage. First negative consequences of substance use encountered.
(5) Adolescent is now physically addicted to a chemical(s), and is trapped in a cycle of compulsive use to avoid withdrawal.	Stage 4: Continued consequences. Substance use continues so that adolescent can feel "normal" again.

³⁶ As many mothers will assert, no matter how old their offspring might become, they are still "my child" or "my baby."

³⁷ Rarely is different from *never*. Some adolescents who use substances do develop a substance withdrawal syndrome, and the probability that they will do so increases in proportion to the period of time that they have used a substance.

Problems in Diagnosis and Treatment of Adolescent SUDs

The first problem is that clinicians lack definitive criteria to identify adolescents for whom substance use has become a problem. Diagnostic standards are derived from those used with adults, although there is strong evidence that these criteria do not automatically apply to children or adolescents (Buckstein & Kaminer, 2015; Kaminer & Buckstein, 2005; Myrick & Wright, 2008; Wagner, 2009). The standards for assessment, diagnosis, and treatment decisions are still in their infancy at best, although progress is being made in this area (Buckstein & Kaminer, 2015; Kaminer & Goodley, 2010; Wagner, 2009).

Having identified a specific child or adolescent who has an SUD places the typical health care professional in a conundrum: First, they lack the tools necessary to separate those adolescents who *misuse* a chemical from those who are *addicted* to that substance.³⁸ Second, a person's substance use behavior can change over time, especially during the turbulent time of adolescence. The adolescent who appears to fit criteria for an alcohol use disorder at the age of 14, for example, might not meet the criteria for a current substance use disorder when he or she is 17 years of age.

Where *loss of control* over substance use is one factor that clinicians look for when working with adults misusing substances, loss of control over substance use expresses itself differently for adolescents.³⁹ Individuals in this age group who have an SUD usually express loss of control through a violation of personal rules ("I will only drink on weekends," or "I didn't *want* to use marijuana last night, but I couldn't help myself," for example). Substance use disorders rarely interfere with job performance for adolescents, since the adolescent's job is usually only a part-time position and the adolescent can usually hide substance use from supervisors. However, their substance use might interfere with their ability to achieve the grades that they would normally be expected to achieve.

Clinicians also usually lack tools to accurately assess the maturity level of the adolescent, the individual's motivation to participate in a treatment program, age-appropriate rehabilitation techniques, or the effectiveness of the rehabilitation program (Knight, 2000; Wagner, 2009). The problem of *access* to a rehabilitation program should not be underestimated: Not even 6% of those meeting the criteria for an SUD were admitted to treatment of some kind, leaving more

than nine out of ten adolescents needing treatment without any (Center for Behavioral Health Statistics and Quality, 2016). There are many reasons for this. For example, states vary as to the legal requirements under which an assessment of adolescent substance use disorders might be carried out. Parental consent might be required in some states but not in a neighboring state. Parental denial⁴⁰ that their child has an SUD is also a problem for the assessor. Many parents and their children view substance use as a sign of moral weakness, making it difficult for them to admit that their child has been misusing chemicals (Corrigan et al., 2005).

Adolescent self-report of substance use is unreliable, as evidenced by the fact that many adolescents admitted to hospital emergency rooms for chest pain vehemently deny the use of cocaine in spite of having cocaine metabolites in their urine. Even in situations where the adolescent is promised confidentiality, they still might under-report their substance use (Stein & Rogers, 2008). To complicate matters, parental reports are not as reliable as drug screens (Roten & Gray, 2015), often for some of the reasons noted above.

Less than a quarter of pediatricians surveyed reported that they felt comfortable assessing an adolescent for a substance use disorder, or in making a referral to a treatment program, and so this issue is often not discussed with the adolescent during a visit to the physician ("Doctors often skip health behavior conversations with teens," 2008). This is unfortunate because research has found that up to 65% of adolescents would like to discuss their substance use with their physician. This might be one reason why less than half of the pediatricians surveyed said that they routinely screen adolescent patients for tobacco, alcohol, or drug use disorders (Winters & Kaminer, 2008). Van Hook and colleagues (2007) identified what they called the "six Ts" that block physician identification and referral of adolescents who use substances: (1) lack of time, (2) lack of training, (3) presence of competing medical problems that require treatment, (4) lack of treatment resources, (5) the tendency for parents to remain in the exam room (making the adolescent less likely to reveal substance use), and (6) the tendency for physicians to lack an awareness of screening tools available to the physician. Despite the American Academy of Pediatrics indication that screening for substance use in adolescents should occur during check-ups, the data above shows that this is not happening in many instances (Roten & Gray, 2015).

The physician, or other health care professional who works with adolescents should review the individual's (Griffin & Borvin, 2010; Myrick & Wright, 2008)

³⁸ A differentiation that is important since intervention for someone with a mild SUD differs from intervention methods employed in treatment of a severe SUD.

³⁹ The CAGE questions, for example, are ill suited for use with adolescents. The CAGE is discussed in more detail in Chapter 28.

⁴⁰ "If we do not allow the assessment to be done, we will not have to face the possibility that our child is using alcohol or drugs."

(a) educational status (including school attendance, academic performance, and disciplinary actions within the school setting, if any), (b) the possibility of loss of control over the substance(s) being used, (c) familial relationships (including possible conflict within the family), (d) peer relationship patterns (substance using peers or non-using peers, for example), (e) legal status (including history of underage drinking citations, arrests for possession of controlled substances, etc.),⁴¹ (f) how the adolescent uses their free time, and (g) history of physical or sexual abuse. Unfortunately, few health care professionals address these issues when they meet with the child or adolescent. Even when they do, they may not be screening with proper methods (discussed next) (Roten & Gray, 2015).

Screening/Assessment Tools⁴²

There is a difference between a *screening* instrument and an *assessment* tool. There are some fairly accurate screening instruments available, as well as a number of well-designed substance use assessment tools for use with children and adolescents. Neither group of instruments is perfect, and there is always room for improvement. In this section, we will look at some of the instruments that have been developed or adapted for use with this population. The gold standard against which both screening and assessment tools are measured is the clinical interview, especially if the assessor establishes an extensive database about the individual (Evans & Sullivan, 2001; Juhnke, 2002; Roten & Gray, 2015). It is necessary to interview each person separately lest the presence of the parents, child, or adolescent prevent the interviewee from being completely honest. Thus, inquiries about possible substance misuse should be made when the parents are not in the consultation room.

Screening Instruments

One of the more popular instruments is the *CRAFT* (Knight et al., 1999), which is a series of questions, available in at least 13 languages, that the adolescent responds to, usually verbally. This includes questions about whether the adolescent has ever been a passenger in a vehicle where the driver was under the influence of chemicals. Other issues addressed are whether the adolescent has used chemicals to

help them relax, forget problems, whether their substance use has ever resulted in psychosocial problems (including family, academic, and legal issues) for the individual, or whether they have used chemicals when alone. The assessor should also inquire whether the child or adolescent has tried to hide the substance use from parents/caregivers. Given that this instrument was specifically designed for use with adolescents, it is preferable to the similar *CAGE* questions (discussed in Chapter 28), which has not shown the validity that the *CRAFT* has with this age group (Roten & Gray, 2015).

A rapidly administered verbal screening instrument is the *TWEAK*, which asks the adolescent about Tolerance, whether others have ever been Worried about their substance use, whether the adolescent has ever used an Eye opener in the morning, or had Amnnesia during periods of substance use, and whether he/she has attempted to cut (K) down on substance use (Johnson, 2003). This instrument may also be used with adults, and is a useful **mnemonic**⁴³ device for the assessor to use with both adolescents and adults.

For cigarette smoking, Doubeni, Li, Fouayzi, and DiFranza (2008) suggested two simple questions: (1) Would it be easy for you to obtain a cigarette? (2) Do you have friends who smoke? A “yes” answer to either question identifies a child who is at high risk for cigarette smoking, and intervention procedures should be initiated, the authors suggest.

The *Drug Use Screening Inventory—Revised (DUSI-R)* (Kircsi, Mezzich, & Tarter, 1995) is a 159-item instrument (protected by copyright) that was designed for adolescents (or adults) who are suspected of having a substance use disorder. The *DUSI-R* only requires about 10 minutes for the individual to complete, and it assesses such potential problem areas as the individual’s (a) substance use behavior, (b) general behavior patterns, (c) health status, (d) psychiatric health status, (e) social skills level, (f) peer relationships, and (g) leisure/recreational habits of the individual. The *DUSI-R* is not diagnostic in itself, but it does identify problem areas that might be addressed in a clinical interview.

The *Drug and Alcohol Problem (DAP) Quick Screen* (Schwartz & Wirth, 1990) was designed for use by physicians in the office setting, and takes approximately 10 minutes. One advantage of this instrument is that it attempts to identify adolescent suicidal thinking, an area of concern since adolescent suicide is a growing problem in society.

Another instrument that is in the public domain is the *Problem Oriented Screening Instrument for Teenagers (POSIT)*, developed by the National Institute on Drug Abuse (NIDA) and the National Institutes of Health (NIH). This instrument is composed of 139 questions that are answered either “yes” or

⁴¹ As marijuana use becomes legalized in a growing number of states, it will become necessary to specifically inquire about the adolescent’s marijuana use, since they might rationalize that since its use is legal for adults, that there is no need to consider its use as reflecting illegal drug use.

⁴² It is not possible to review every screening or assessment instrument available. This summary is limited to some of the more popular or better-designed instruments, in the opinion of this author.

⁴³ See Glossary.

“no” by respondents 12–19 years of age. The individual’s response pattern provides information on his/her (a) substance abuse patterns, (b) physical health, (c) mental health, (d) family relations, (e) peer relations, (f) educational status, (g) social skills, and (h) aggressive behavior or delinquency tendencies. Identified problem areas are then examined in more detail through clinical interviews with the client.

One of the more popular instruments used when assessing an adolescent is the adolescent version of the *Substance Abuse Subtle Screening Inventory-3* (SASSI-3) (Juhnke, 2002). This instrument is used with adolescents 16 years of age or older, who have at least a fourth-grade reading level. The SASSI-3 is discussed in more detail in Chapter 28, but the reader should be clear that an adolescent version of this instrument does exist, and might be used to help assess the adolescent client.

The *Adolescent Drinking Index* (ADI) is occasionally used by assessors, although there is limited data on its effectiveness, especially with adolescents who attempt to minimize their alcohol use (Stein & Rogers, 2008). Another instrument that is occasionally used when assessing adolescents for possible substance use disorders is the *Adolescent Drug Abuse Diagnosis* (ADAD) test. It attempts to measure nine different areas of the adolescent’s life and then rate the degree of distress caused by substance abuse in each of these domains. This instrument can also be used to assess pretreatment and post-treatment changes for the adolescent (Johnson, 2003).

Finally, the *Teen Addiction Severity Index* (TASI) is occasionally used by assessors attempting to interpret an adolescent’s substance use pattern. However, the normative samples for this instrument were small, and generalizability to the general adolescent population is open to question (Stein & Rogers, 2008).

Although it is not possible to discuss every screening instrument, there are a number of instruments available to the assessor. Each of these instruments has flaws and limitations, and the data provided by each test should be interpreted with caution. However, each also provides information that might be of value in identifying the child or adolescent who is misusing substances.

Possible Diagnostic Criteria for Children or Adolescents with Suspected SUDs

To aid the assessor during the clinical interview portion of the assessment process, the following are offered as possible indicators of a potential substance use disorder in either a child or adolescent:

Children

Zucker and colleagues (2009) warned that the “predictors” of possible substance use disorders in children or adolescents must be viewed as probabilities rather than firm indications of the existence of an SUD in either age group. With this warning in mind, some of the identified risk factors for childhood alcohol use include (Levi et al., 2015; Meyers & Dick, 2010; Millar, 2009; Zucker et al., 2009):

- Having a friend or close sibling who uses alcohol or drugs
- Internalizing feelings instead of expressing them
- Externalization of feelings
- Social problems
- Poor impulse control
- Engaging in risk-taking behavior(s)
- Poor parental supervision and/or inconsistent discipline
- Trauma (including parental divorce)
- Victimization
- Poor academic performance
- Problems controlling temper outbursts
- Parental alcohol use disorder
- Caucasian heritage

The issue of internalization versus externalization as predictors of a possible substance use disorder in children would initially appear to be contradictory. However, each identifies a different pattern of risk factors that applies to different subpopulations of children (Zucker et al., 2009). Children who tend to externalize also tend to demonstrate poor emotional and behavioral self-control, possibly finding full expression in those children diagnosed as having a conduct disorder (Zucker et al., 2009). In contrast, children who tend to internalize tend to experience anxiety, depression, shyness, and excessive inhibition, according to Zucker and colleagues (2009). It should be noted, however, that the indicators of children with an SUD are limited, in part because of a lack of research in this area.

Adolescents

There is no single characteristic profile to warn parents that their adolescent child is at high risk for misusing alcohol and/or drugs. Every adolescent is unique, and thus will present the assessor with a unique combination of strengths, weaknesses, and needs (Johnson, 2003; Thatcher & Clark, 2008; Weiner, Abraham, & Lyons, 2001). While not definitive, the following are characteristics that hint at an increased risk of a substance use disorder for adolescents (Clark et al., 2002; Crowley, 2007; Evans & Sullivan, 2001; Johnson, 2003; Kaminer, 2008; Kirisci, Vanyukov, & Tarter, 2005; Kriebbaum

& Zernig, 2000; Meyers & Dick, 2010; Miller, Davies, & Greenwald, 2000; Perekh, 2006; Wills et al., 2001; Zuckerman, 2012):

1. Familial history of SUDs
2. Affective illness
3. History of suicide attempts
4. Loss of loved one(s)
5. Low self-esteem
6. High levels of stress
7. Poor social skills/maladaptive coping skills, social isolation
8. Troubled relationship with parents (either 9 or 10 of list, below)
9. Parental permissive attitudes towards deviant behavior, or
10. Overly strict parental behaviors towards deviant behaviors
11. Adolescent coming from a single parent or blended family
12. Feelings of alienation or running away from home,
13. Low commitment or low expectations for school
14. Early use of cigarettes
15. High levels of involvement with drug-using peers
16. Antisocial behavior (or conduct disorder)
17. Poor impulse control
18. Early sexual experience, including high-risk sexual activities
19. Early experimental substance use
20. Legal problems during adolescence
21. Absence of strong religious beliefs
22. Unsuccessful attempts to stop or cut back on substance use
23. History of substance withdrawal
24. Having experienced one or more alcohol-induced "blackouts"
25. Continued substance abuse in spite of consequences
26. Use of chemicals prior to or during school

The greater the number of the above criteria that apply to a given individual, the greater the odds are that he or she has a substance use disorder. However, adolescent substance use patterns are highly variable. Suris, Akre, Berchtold, Jeanin, and Michaud (2007) found that there were different subgroups of adolescents who use marijuana. The authors found that some adolescents who use marijuana did not use tobacco products at all. Such adolescents were more likely to (a) be involved with sports activities, (b) be in an academic tract, and (c) have higher academic achievement levels, as compared with adolescents who used both marijuana and tobacco products.

It should be apparent by now that there is little consensus on the diagnostic criteria to apply to possible substance

misuse in children or adolescents. Identified risk factors are vague, and many children or adolescents who have several identified risk factors will never use or misuse alcohol or drugs. In the next section we will review the possible health and psychosocial consequences of a substance use disorder in a child or adolescent.

Consequences of a Substance Use Disorder in a Child or Adolescent

It is not possible to identify every negative consequence that a child or adolescent misusing substances might experience. What follows is a brief overview of the specific consequences that might result from the misuse of specific substances in childhood or adolescence. Little is known about the effects of polydrug misuse in children or adolescents, although this is a common practice among certain groups.

Alcohol

Although binge drinking in adolescents seems to be on the decline since a peak in 1979, alcohol use is still a significant concern (Johnston et al., 2017). One-third of high school seniors and one-fifth of high school sophomores indicated use of alcohol in the last month when surveyed in 2015 (Johnston et al., 2017). Unfortunately, in using alcohol, the child or adolescent becomes vulnerable to most of the undesired effects of alcohol use discussed in Chapter 5. Admittedly, it is unlikely that the child or adolescent will develop conditions such as cirrhosis of the liver frequently found in who are older, and have more chronic drinking patterns; however, acute alcohol poisoning is a real possibility.⁴⁴ While adolescents are unlikely to develop esophageal varices due to their drinking, it is possible that their alcohol use will interfere with academic performance or cause accidental injury. Alcohol-related high-risk decision making is also a problem, resulting in unplanned pregnancies and exposure to sexually transmitted diseases.

There is a lack of objective data on how child and adolescent alcohol use might affect the physical or emotional growth of the individual. However, anecdotal evidence suggests that the misuse of or an addiction to alcohol interferes with the individual's emotional growth: The individual is thought to stop growing emotionally at the age when they begin heavy use of alcohol. This is a potential relapse trigger later in life: Imagine a 22-year-old newly abstinent adult

⁴⁴ Every year there are reports of a high school or college student who died from an acute alcohol overdose after drinking at a school party.

facing life's problems using the emotional resources of a 13-year-old! The individual who is in such a situation might be tempted to return to the oblivion promised by alcohol.

Although it is known that alcohol is a neurotoxin, the effects of alcohol misuse on the neurological maturation of a child or adolescent is still under investigation. Preliminary evidence does suggest that adolescent girls are more vulnerable to the neurotoxic effects of alcohol than boys because of neurological differences between the two sexes (Rutherford et al., 2010). Gray matter reduction and other neurological abnormalities have been surfacing in the research on adolescents who drink heavily (Squeglia & Gray, 2016). Additionally, it seems that alcohol use and withdrawal may result in problems with verbal learning skills and memory (Squeglia & Gray, 2016). There is a need for more research in this area.

Benzodiazepines

There is virtually no research into the effects of intentional benzodiazepine misuse on childhood or adolescent neurological or psychosocial development. Children and adolescents who misuse benzodiazepines may be at risk for all the dangers mentioned in Chapter 7.

Cocaine

Children and adolescents who use cocaine run the risk of the potential dangers of cocaine discussed in Chapter 9. Unfortunately, many children and adolescents mistakenly believe that you cannot become addicted to intranasal cocaine, a misperception often abetted by those who sell the cocaine to the user. Those who misuse cocaine are at increased risk of contracting hepatitis C, as discussed in Chapter 36. If the individual uses intravenous cocaine and shares needles, he or she is also vulnerable to not only the infectious diseases discussed in Chapter 36 but also a host of other blood-borne pathogens.

Unfortunately, there has been little age-specific research into possible damage of cocaine use to the child or adolescent's neurological or psychosocial development. It is known that individuals who do misuse cocaine in childhood or adolescence are vulnerable to cocaine-induced strokes or the cardiac dysfunctions discussed in Chapter 9, as well as to the other complications that can result from the use of this substance.

Hallucinogens

There has been limited objective research into the effects of the various hallucinogenic compounds on the growth and development of children or adolescents, which is surprising

since hallucinogen use is most common in the under-25 age cohort. However, it has been observed that compounds like MDMA are capable of causing memory disturbances, which may be permanent. Children and adolescents who use these compounds do put themselves at risk for any of the negative consequences associated with the use of these compounds, as discussed in Chapter 12.

Inhalants

Although children and young adolescents are the age cohorts that most commonly use inhalants, there has been little systematic research into how the use of these compounds might influence neural growth and development in these age groups. Many of these compounds are neurotoxic, have the potential to trigger cardiac arrhythmias, or both, making their use at any time potentially dangerous. Specific dangers associated with the use of hallucinogenics are outlined in Chapter 13.

Marijuana

Researchers believe that 4.5 million teenagers used marijuana in 2015, exposing them to the endocannabinoid-like chemical THC. One function of the **endocannabinoids**⁴⁵ is to guide neural growth during the development of the cortex. This region of the brain is still in development during childhood and adolescence. Although few adolescents view rare marijuana use (circa one time a month) as dangerous, even such limited marijuana use holds the potential to interfere with normal neurocognitive development (Gold & Dupont, 2008; Squeglia & Gray, 2016). The long-term implications of adolescent marijuana use are still being explored, but animal-based research suggests that marijuana use during adolescence might permanently alter serotonin and norepinephrine levels in the adult brain (Bambico, Nguyen, Katz, & Gobbi, 2009). Theoretically, this could lead to increased anxiety and depression in adults who engaged in daily marijuana use in adolescence; however, this has not been investigated yet. Additionally, research is indicating that marijuana use during adolescence can have significant negative short-term impacts on numerous cognitive factors, such as attention, memory, processing speed, and cognitive control (Squeglia & Gray, 2016). When use is stopped, it seems that attention challenges may continue and that neurological impacts may still be present after abstinence, although further research is needed in these areas (Squeglia & Gray, 2016). Further, between 33 and 40% of adolescents who smoke marijuana daily will become addicted to it (Crowley, 2007; Gruber & Pope, 2002). Many of

⁴⁵ See Glossary.

these individuals continue to use marijuana in part to avoid withdrawal symptoms,⁴⁶ a fact that may have lifelong consequences for that individual's cortical development.

Marijuana use disorder (MUD; alternatively, cannabis use disorder, CUD) in the 15-year-old manifests itself differently, follows a different path, and might have different neurobehavioral consequences than a MUD in a young adult (Ellickson, Martino, & Collins, 2004). One characteristic that might identify adolescents with an MUD is that they started to use it prior to the age of 16, and that they report having positive experiences when they first used it (Ferguson, Horwood, Lunskey, & Madden, 2003). However, criteria to help identify the adolescent or young adult with a CUD are still in the early stages of development, and the assessor must rely on more traditional criteria outlined earlier in this chapter.

Methamphetamine

The consequences of methamphetamine use in childhood or adolescence have not been explored in depth. It is known that stimulant use seems to impact both memory and visual learning (Squeglia & Gray, 2016). The child or adolescent who uses these compounds risks any of the adverse consequences inherent in the use of methamphetamine (discussed in Chapter 8), which may be permanent. Anecdotal evidence would suggest that adolescents often begin to use methamphetamine intranasally and dismiss the addictive potential of the drug in the mistaken belief that it is not addictive if you snort it. Children or adolescents who share needles are also vulnerable to the various blood-borne infections inherent in this practice, some of which are discussed in Chapter 36.

Tobacco

Tobacco use is illegal in many states for persons under the age of 18, with a recent increase to 21 by some states and communities (Preventing Tobacco Addiction Foundation, 2017). This belies the fact that more than 4.7 million middle and high school students indicated use of tobacco in 2015 (Singh et al., 2016). In 2016, one out of ten eighth-graders started to smoke (Johnston et al., 2017).

These statistics are more frightening in light of an emerging and quite impressive body of evidence that supports the argument that the tobacco industry is actively manipulating the menthol levels in cigarettes, with the intention of enticing adolescents and younger adults to begin smoking. Menthol levels used to cover the harsh taste of cigarette

smoke were found to be more attractive to adolescents than non-menthol brands, thus acting as an incentive for the adolescent or young adult to begin smoking, the authors suggested (Kreslake, Wayne, Alkpert, Hoh, & Connolly, 2008). There is also evidence that adolescents tend to be unaware of the signs of an emerging nicotine-dependence problem, increasing their risk for an addiction to nicotine as they continue to smoke (Doubeni, Reed, & DiFranza, 2010).

Opioids

The diversion of prescribed narcotic analgesics has become a major problem for adolescents in the past decades, a problem fueled by the myth that narcotic analgesics are not addictive if ingested orally or if one is taking pharmaceuticals. The age of peak risk for the initiation of non-prescription narcotic use is 14–16 years, although there are smaller peaks in the incidence of non-prescribed narcotic analgesic abuse at 12–14 and again at 19–21 (Meier, Troost, & Anthony, 2012; Parker & Anthony, 2015). That adolescents believe such myths is unfortunate since an estimated 120 adolescents become addicted to narcotics each day (Parker & Anthony, 2015). This would suggest that psycho-educational education programs that focus on the 12–14 age cohort might be attempting to intervene *after* the adolescent has started to form attitudes about narcotic analgesic use, if not actually started to misuse them (Meier et al., 2012). Further, Zhang and colleagues (2008) examined the rate of oxycodone self-administration by adolescent as opposed to adult mice and found a significantly higher rate of self-administration in adolescent mice. This would suggest that the adolescent mice in this study seemed to be more vulnerable to the reinforcing effects of oxycodone than are adults. This study has not been replicated using human subjects, but it does have implications for therapists working with adolescents who misuse opiates.

In cases of adolescent opioid use disorder, the standard treatment has been a two-week taper from opioids using an opioid agonist such as buprenorphine, combined with psychosocial counseling (Woody et al., 2008). The authors examined the use of longer-term (12 weeks) use of buprenorphine-naloxone, followed by detoxification using a number of opioid-free urine toxicology tests and patient retention as treatment measures, and concluded that this approach was more effective than the standard 2-week detoxification sequence combined with substance rehabilitation counseling. However, the authors also found that by the end of 12 weeks the number of adolescents who remained in treatment was approximately the same as for those who received the standard treatment. Additional evidence points to the use of methadone first with adolescents who have been injecting opioids

⁴⁶ Discussed in Chapter 10.

(Srivastava, Kahan, & Nader, 2017). It is recommended that safety be considered first, then treatment retention, for the detoxification process (Srivastava et al., 2017).

Other Compounds Misused by Children and Adolescents

There are continually new examples of compounds misused by children and adolescents, many of which they might read about or see through internet sources. The extent of and long-term consequences of use of these compounds are often not known until significant levels of individuals are harmed or die from the use.

Adolescent Rehabilitation Programs

Having identified an adolescent with a substance use disorder serious enough to warrant admission to a rehabilitation program, the assessor must choose a treatment setting. This in itself is a difficult task since there is a “shocking” (Bukstein & Kaminer, 2015; Trivedi, 2010, p. xiii) dearth of treatment programs to which an adolescent might be referred. Combined with the lack of training for health care professionals who wish to work with this specialized population, only 10–15% of adolescents in need of professional assistance for a substance use disorder receive such help (Kaminer, 2010). Fewer than one-third of rehabilitation programs surveyed offered treatment for adolescents, and the quality of such programs is on average only fair (Knudsen, 2009). Approximately 80% of these adolescent rehabilitation programs are outpatient programs (Kaminer & Goodley, 2010), and there is a decided lack of residential treatment programs for adolescents with an SUD (Kaminer, 2008). To complicate matters, few adolescent treatment programs for substance use disorders or behavioral issues seem to be effective (Dobbs, 2011), although treatment has been generally shown to be better than not receiving treatment (Bukstein & Kaminer, 2015). Despite a push by the American Society of Addiction Medicine (ASAM) to match people with treatment, there are not enough options for this to be effective with this age group (Bukstein & Kaminer, 2015). The assessor is thus often forced to accept a less-than-desirable treatment setting for the adolescent misusing substance because of a lack of access to better programs.

Even if the assessor is able to arrange for a given child or adolescent to enter a substance rehabilitation program, there are many factors that can interfere with the effectiveness of treatment. Some of these factors include (a) unrealistic parental expectations, (b) hidden agendas for treatment by both the adolescent and parents, (c) parental psychopathology, and (d) parental substance use. While it is useful to include the

parents and family members in the treatment program, often they refuse to participate in the rehabilitation efforts. An example of points (c) and (d) above is found in the observation that even parental smoking has been found to influence the substance use patterns of the adolescent, suggesting that parents lose credibility when they try to prevent adolescent substance use disorders if they are themselves engaging in the use of a substance, even if it is “just” cigarette use (Keyes, Legrand, Iacono, & McGue, 2008). Fletcher (2013) also noted that parental attitudes about having an adolescent in treatment vary, but might be a source of shame for the parent.

The Special Needs of Adolescent Substance Rehabilitation Programs

In contrast to more traditional rehabilitation programs that work with adult clients, the adolescent’s cognitive abilities, strengths, weaknesses, and defensive style will evolve over the course of treatment as the child matures. Further, treatment must address ancillary issues such as sexually transmitted diseases, birth control, and vocational needs, issues that might make the parents uncomfortable. The adolescent’s cultural heritage should be a consideration in any rehabilitation program. A diverse treatment program staff or enlistment of ancillary staff from that individual’s culture will enable the adolescent to find at least one person to identify with during their participation in a rehabilitation program.

It is also necessary to match the individual with a treatment approach based on the adolescent’s personality. Conrad and colleagues (2013) trained a number of teachers, school counselors, and other educational professionals in selected schools in both cognitive-behavioral and motivational interviewing techniques and found that when the educators were able to match the interventional approach to a specific student based on their personality, they were able to achieve a 29% reduction in drinking as compared with the control group over the 2 years the students were followed. This would suggest the possibility that one reason why adolescent rehabilitation programs are so often ineffective is that there is a conflict between the child’s personality and the treatment approach.

A potential source of treatment failure and parent–child conflict is the common mistake of viewing the adolescent’s physical size as an indicator of emotional or intellectual maturity. During the rehabilitation process, treatment center staff need to consider the individual’s level of cognitive maturity when working with the adolescent. Adolescents and adults process environmental stimuli differently: Adolescents benefit from a here-and-now focus rather than focusing on possible long-term consequences of their behavior(s) (Brook, 2008). Adolescents underestimate risk and over-anticipate rewards for substance use (Hopson, 2013; Roten & Gray,

2015; Rutherford et al., 2010). Thus, those regions of the brain responsible for “top-down” behavioral inhibition are still maturing, while those regions of the brain involved in the reward cascade are fully functional (“bottom-up” control).

Group therapies designed to work with adults with an SUD, long a mainstay in most rehabilitation programs, are sometimes viewed as not appropriate for adolescents (Bukstein & Kaminer, 2015). The group therapy format must be modified to work with adolescents (Fletcher, 2013) but can generally be considered effective and safe for this age group (Bukstein & Kaminer, 2015). However, adolescents should not be referred to mixed-gender therapy groups because of the differing developmental issues for either sex during this phase of life (Brook, 2008). A given adolescent might be reluctant to discuss personal problems if there are members of the opposite sex in the same group and might prefer to discuss these matters in individual psychotherapy with a properly trained mental health professional.

Group therapies with adolescents are more challenging than are such therapies with adults with SUDs. Confrontation and feedback are often more readily accepted if offered by a peer rather than a staff person, underscoring the difference between adolescent and adult substance rehabilitation therapy groups. The group leader must assume a more active role in setting limits with adolescents in a treatment group (Brook, 2008). Unfortunately, members of adolescent therapy groups often become enamored with the “war stories” that other group members tell of their drug experiences (“Does teen drug rehab cure addiction or create it?”, 2010). It is the counselor’s job to steer the group away from such discussions. Adolescents should not be involved in therapy groups for adults with SUDs (Fletcher, 2013). The information processing systems of adolescents differ from those of adults, providing ample grounds for misunderstanding and disruption in a group, and there is a danger that the older group members might try to take advantage of the adolescent group member. Further, the adolescent’s need for problem-solving training usually differs from that of an adult who misuses the same compound. Finally, the family therapy format must be modified to address each adolescent’s unique place in the family constellation, as well as potential problems such as parental substance use.

Adolescent involvement in the juvenile criminal justice or child protection systems are unique, and treatment staff should include these agencies in the individual’s rehabilitation program.⁴⁷ Finally, the adolescent’s social support system must be examined and if necessary modified. Adolescents who had at least one nonusing peer and who remained in treatment

or aftercare for approximately a year were found to be less likely to relapse (Latimer, Newcomb, Winters, & Stinchfield, 2000). Adolescents who did relapse often did so as a result of social pressure. When there are 12-step programs available for adolescents, such groups might provide a useful adjunct to the rehabilitation program. The rehabilitation process should be sufficiently long and intense to adequately address identified problems during the adolescent’s time in a treatment program. Additionally, aftercare is essential to improving long-term outcomes (Bukstein & Kaminer, 2015).

Further, like their adult counterparts, adolescents who do use alcohol or illicit drugs may minimize their substance use, especially if they believe that this information might be used against them. They might admit to the use of “one or two beers,” for example, without revealing that the beer cans are 40-ounce cans⁴⁸ and not the more traditional 12-ounce cans (Rosenbloom, 2005). This underscores the need for a multidisciplinary assessment of the individual to allow for accurate identification of the client’s strengths, weaknesses, the stage of substance use the individual is at, and her or his level of maturity and adaptive style, so that the staff might better understand how to work with the client. Finally, those working with adolescents should be aware of the unique effects of the drugs of misuse on the adolescent, as previously discussed in this chapter.

Referral Sources

Referrals for substance treatment come from many different sources. The juvenile court system, and especially the emerging “drug court” program, will often refer an offender for evaluation with the stipulation that the adolescent also follow treatment recommendations. School officials will often refer a student suspected of substance use for assessment, and it is not unusual for parents to make such referrals, especially in strict homes where even the first hint of substance use is not tolerated. The phenomenon of home urine drug tests has contributed to this process, although possibly at the cost of damaging parent–child trust. Parents rarely understand that a positive urine toxicology test does not automatically indicate illicit substance use or that false positive results might be possible. Even if the test does accurately identify illicit drug use, this does not in itself prove that the child or adolescent is *addicted* as opposed to having simply used a given compound, or that there is then a need for rehabilitation, although this might indicate the need for an assessment of the adolescent’s substance use pattern by a properly trained counselor (Winters & Kaminer, 2008).

⁴⁷ The reader is advised to consult with an attorney familiar with the laws in his or her state to determine the child or adolescent’s rights if referred to such a program prior to making the referral.

⁴⁸ Sometimes referred to as “silos” or “tall boys” by the drinker.

Adolescent Substance Use Treatment: A Cause for Optimism?

There is strong evidence suggesting that for every year adolescents delay the initiation alcohol or prescription drug misuse, the risk for developing a future substance use disorder drops 5% (McCabe, West, Morales, Cranford, & Boyd, 2007). Further, adolescents with alcohol use disorders who are referred to a rehabilitation program appear to benefit more than adults who are referred to a similar program (Kriechbaum & Zernig, 2000). Behavioral therapies, including motivational interviewing (MI), appear to be at least moderately effective with adolescents using substances, although the program must be modified to meet the adolescent's needs (Macgowan & Engle, 2010). Further, in many cases, psychological trauma that motivates an adolescent to misuse chemicals is easier to assess through psychosocial interventions than in adults (Jorgensen, 2001). Finally, although many parents fear the worst, the heavy misuse of alcohol or illicit drugs is often limited to adolescence (Kaminer, 2008). Only a minority of those adolescents who briefly use a chemical continue on to develop a substance use disorder later in life (Kriechbaum & Zernig, 2000; Larimer & Kilmer, 2000).

Is There a Financial Incentive for Over-Diagnosis?

Many treatment programs for adolescents are “for profit.” To maximize profits, some admissions officers blur the line between adolescent substance use, misuse, and addiction, especially given the recent combination of previous categories in the *DSM-IV* into one broad category of substance use disorder in the *DSM-5*. It is not unheard of for an adolescent treatment program to offer a “one-size-fits-all” diagnostic assessment and a similar style of treatment (Weiner et al., 2001). Many adolescent substance rehabilitation professionals maintain that treatment for the adolescent is automatically a positive, growth-enhancing experience, a belief that is untrue: An unknown percentage of adolescents are *harmed* by intervention or treatment programs (Fletcher, 2013; Szalavitz, 2006). The analogy of surgery might not be out of place here. If a surgeon were to advocate abdominal surgery, stating that it is automatically a healthy thing for people to do, she or he would be charged with criminal intent and malpractice in short order.

There are adolescent treatment programs where the staff attempt to convince the parents that the adolescent will be permanently impaired because of the assumed SUD, and that the adolescent or their families can never be emotionally “whole” without treatment. Lamentably, there is no research to support this philosophy, just as there is no evidence that

telling the adolescent that he or she is a lifelong addict is either true or healthy for the adolescent. Indeed, there is anecdotal evidence that being told by staff that the adolescent is a drug addict or alcoholic cements the individual's identity as such (“Does teen drug rehab cure addiction or create it?” 2010). Such programs ignore research evidence suggesting that the majority of adolescents identified as having an SUD do not continue down the path to chemical addiction (Kaminer & Buckstein, 2005). Thus, when making a referral to a substance rehabilitation program that works with children or adolescents with a substance use disorder, let the buyer beware.

The legal framework within which the parents and the assessor must work varies from state to state. In some states, the adolescent can refuse to enter treatment if he or she is above a certain age. In other states, the adolescent can be forced into a rehabilitation program by the parents without his or her consent (Evans & Sullivan, 2001). Some states allow the adolescent to refuse to let parents see his or her treatment chart, while in other states the child or adolescent has no such privilege. The assessor should consult with an attorney to discuss the legal requirements and restrictions for a rehabilitation counselor working with children or adolescents.

The Danger of Under-Diagnosis

There is strong evidence that the majority of adolescents misusing substances are never identified as such (Evans & Sullivan, 2001; Lee, Garnick, Miller, & Horgan, 2004). The implications of this failure are staggering: For example, substance use disorders are a significant part of the problem of adolescent suicide (Miller et al., 2006; Simkin, 2002; Weiner et al., 2001). Some of the other risk factors for adolescent suicide include⁴⁹ (a) adolescent affective disorders, (b) thoughts of suicide by the adolescent, (c) a family history of depression or suicide, (d) impending court or legal problems, (e) thoughts about joining a deceased loved one, and (f) having easy access to a handgun (Simkin, 2002; Sorter, 2010). Adolescent substance misuse contributes to disinhibition and high-risk behavior(s), which are in turn a major factor for adolescent accidental injuries (Miller et al., 2006). Approximately 40% of adolescents treated in one hospital emergency room had evidence of drugs or alcohol in their urine (Erlich, Brown, & Drongowski, 2006). It has been hypothesized that these behaviors reflect the belief by adolescents that they are invulnerable, or that bad things do not happen

⁴⁹This list is hardly comprehensive. The topic of adolescent suicide is the subject of many books, and the reader is referred to one of the many books or research articles on this subject.

to them. Another complication is that about 15% of adolescents believe they will die at an early age. The authors found that almost 11% of their sample thought that they had only a 50% chance of living to the age of 35.⁵⁰ However, while this information was used to guide medical treatment for the injured adolescent, it was found to rarely result in a referral for assessment and possible treatment. However, an accidental injury or high-risk behavior might be one of the first signs that the adolescent might have an SUD.

The professional interacting with children and adolescents must find a middle ground between over-diagnosis and under-diagnosis, a process that is difficult at best, and possibly impossible. However, this dilemma does underscore the need for accurate diagnostic criteria to identify adolescent substance users. The current *DSM* criteria may not be appropriate for evaluating these age groups, as those meeting only a few criteria could be engaging in what might be considered normal for their developmental stage (Bukstein & Kaminer, 2015).

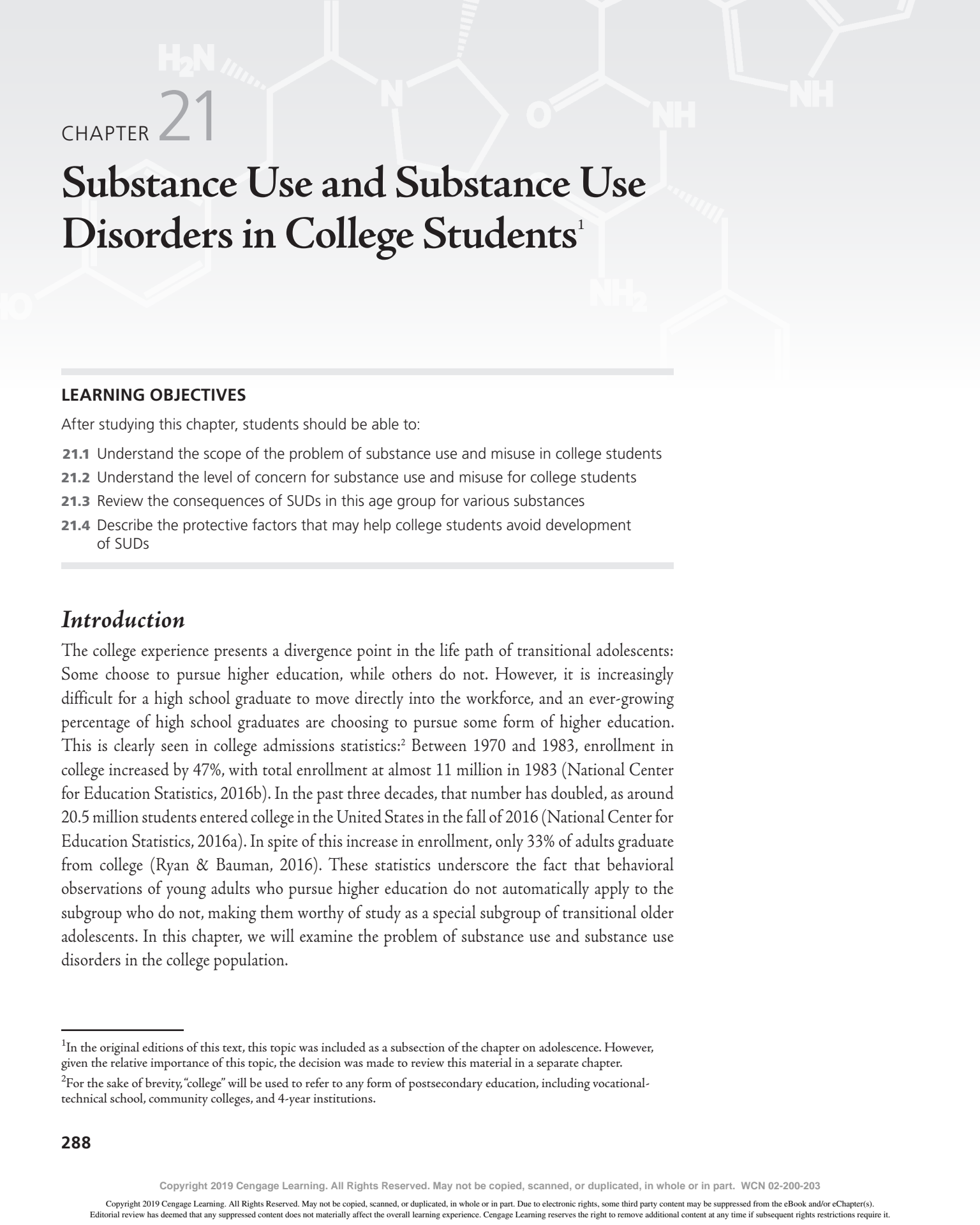
Chapter Summary

Although society has reawakened to the problem of child and adolescent substance use and SUDs, there remains a lack of serious research into the problem or its solution(s).

⁵⁰The examiner should take time to explore *why* the adolescent believes this. For many gangs, for example, early death is the norm and not the exception. Another example might be seen in the hypothetical adolescent from a family where many members died before the age of 35 from cancer; their belief that they might die at an early age might not be unreasonable.

It is known that peer pressure, the media's portrayal of substance use, parental substance use, and self-esteem are all intertwined and play a role in the adolescent's decision to begin, and to continue, substance use, yet the exact role of each of these forces is not known. Still, child or adolescent substance use can have lifelong consequences. A cocaine-induced stroke at the age of 17 does not resolve when the adolescent turns 18 or 21, for example. Injuries sustained in an alcohol-related motor vehicle accident, even if the adolescent was only a passenger, will have lifelong implications for the individual's health and development.

In the face of a dearth of clinical research to guide the treatment professional, it is necessary to steer a cautious path between over-diagnosis and under-diagnosis of a substance use disorder. Just as is true for surgery, the treatment professional must weigh the potential benefits against the possible harm from this process, and there is indeed a potential for harm from an intervention effort that is poorly executed or forced on an adolescent who has engaged only in experimental substance use. Many adolescents "mature out" of their substance use as they reach young adulthood (Szalavitz, 2006). Others continue to misuse chemicals in a problematic way. The diagnostic criteria to identify those who are more likely to continue to develop a substance use disorder are still lacking. Thus, the treatment professionals have no established principle to guide them in their efforts to identify, assess, or treat children or adolescents with substance use disorders. This is an evolving area of pediatric medicine, and health care professionals must attempt to assess and treat children and adolescents who misuse substances while the guidelines for assessment and treatment are still being developed. This remains a daunting challenge.

A faint, light gray chemical structure diagram of a complex organic molecule, possibly a neurotransmitter or a drug, is overlaid on the page. It features various functional groups including amine (H2N, NH), amide (NH-C=O), and hydroxyl (OH) groups, along with a benzene ring and several other rings and bonds.

CHAPTER 21

Substance Use and Substance Use Disorders in College Students¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 21.1** Understand the scope of the problem of substance use and misuse in college students
- 21.2** Understand the level of concern for substance use and misuse for college students
- 21.3** Review the consequences of SUDs in this age group for various substances
- 21.4** Describe the protective factors that may help college students avoid development of SUDs

Introduction

The college experience presents a divergence point in the life path of transitional adolescents: Some choose to pursue higher education, while others do not. However, it is increasingly difficult for a high school graduate to move directly into the workforce, and an ever-growing percentage of high school graduates are choosing to pursue some form of higher education. This is clearly seen in college admissions statistics:² Between 1970 and 1983, enrollment in college increased by 47%, with total enrollment at almost 11 million in 1983 (National Center for Education Statistics, 2016b). In the past three decades, that number has doubled, as around 20.5 million students entered college in the United States in the fall of 2016 (National Center for Education Statistics, 2016a). In spite of this increase in enrollment, only 33% of adults graduate from college (Ryan & Bauman, 2016). These statistics underscore the fact that behavioral observations of young adults who pursue higher education do not automatically apply to the subgroup who do not, making them worthy of study as a special subgroup of transitional older adolescents. In this chapter, we will examine the problem of substance use and substance use disorders in the college population.

¹In the original editions of this text, this topic was included as a subsection of the chapter on adolescence. However, given the relative importance of this topic, the decision was made to review this material in a separate chapter.

²For the sake of brevity, “college” will be used to refer to any form of postsecondary education, including vocational-technical school, community colleges, and 4-year institutions.

Why Worry About College Substance Use?

The answer to this question is relatively straightforward:

- More than 1,825 college students die and nearly 600,000 are injured while intoxicated (Miller, 2013; White & Hingson, 2014).
- Ninety-seven thousand college students are the victims of alcohol-related sexual assault, or “date rape” experiences each year. In over 90% of these rapes, the victim knew the perpetrator (Miller, 2013).
- Approximately 25% of college students admit that their use of alcohol has caused academic problems for them in college³ (Miller, 2013; White & Hingson, 2014).
- An estimated 650,000 college students are involved in an alcohol-related fight each year (White & Hingson, 2014).
- Fifty-nine percent of off-campus fires involve alcohol, with approximately 10 students per year losing their life in these fires.
- Conservative estimates are that approximately 20,000 college students are hospitalized each year for having overdosed either on alcohol alone or on alcohol combined with another substance (White & Hingson, 2014).

The relationship between substance use and accidental injury is quite complex. Male college students were 19% more likely to suffer an injury for each day they consumed more than eight drinks, while female college students were 10% more likely to suffer an injury for each day they consumed five or more drinks (Mundt, Zakletska, & Flemming, 2009). A third of women who end up with alcohol-related injuries may have avoided them if there was no heavy drinking involved (Caamaño-Isorna et al., 2017). Since alcohol use is often viewed as a rite of passage within the college community, alcohol use disorders are *three times as common as in the general population* (National Institutes of Health, 2017).

A Special Environment

The phase of life known as *young adulthood* has been divided into subphases: that of early young adulthood, a transitional period between adolescence and young adulthood

traditionally that begins at about the age of 18 and ends at around the age of 21–22 years of age. Middle young adulthood usually begins at about the age of 21 and continues until the age of 29, and the last phase of young adulthood traditionally is viewed as starting at about the age of 29 and continuing until the midlife transition. Those who elect postsecondary education usually do so during the transitional phase into young adulthood and graduate during the middle young adult years. The on-campus college experience provides transitional adolescents⁴ or young adults⁵ a unique environment: Students are to some degree protected from the larger society within which they exist. Within the sheltered environment of a postsecondary educational facility, a sense of community membership evolves both in students who reside on-campus⁶ and those who reside off-campus.⁷ The institution provides an isolated environment in which there is minimal parental supervision⁸ for the most part, but in which the student is faced with unique academic, behavioral, interpersonal, developmental, and financial demands (Winters et al., 2012). Their ability to adapt is both tested and often rewarded with opportunities that do not exist outside of the postsecondary campus environment.

The college experience forces the high school graduate to attempt multiple tasks simultaneously: (a) learning to function independently in a challenging academic environment, (b) developing supportive social networks, and (c) possibly dealing with the feelings that follow separation from home for extended periods. During this phase of life, the individual's relationship with their parents will also evolve, and often areas of conflict are outgrown as parents assume the new role of mentors in the young adult's life (Brown et al., 2009). As the college student makes this transition, his or her relationship with alcohol and illicit drugs also changes. This is not a static process, but continues throughout the college years and overlaps with the other tasks outlined above.

Peer Relationships

For the majority of college students, their high school peer relationships will either dissolve or assume new forms.

⁴A term which, in this text, refers to the 18–21 age cohort.

⁵For the sake of this chapter, young adult is defined as between 20 and 29 years of age.

⁶A term that includes those who live in fraternities or sororities (“Greek”) houses, as well as college dormitory units.

⁷Apartments shared with others, or living with parents or relatives and commuting to classes, etc.

⁸Surprisingly, even after the student moves into the dormitory or fraternity/sorority house, perceived parental awareness of their alcohol use and the expression of care and concern about the student's drinking influences their alcohol use.

³For example, having a “hangover” the day that the student has to take an exam, resulting in a lower grade than he or she would normally achieve on that test.

College students begin the process of building a peer relationship support system consistent with their expectations and goals for college. Those students with the strongest motives for attending college are typically more likely to reach out to others with similar values and least likely to misuse alcohol or recreational drugs, since this would interfere with their academic goals. This is seen in the fact that although 1.4% of young adults report having used heroin, only 0.4% of college students report doing so (Johnston, O'Malley, Bachman, Schulenberg, & Miech, 2015b). Unfortunately, a subpopulation of undergraduates turn to alcohol or other drugs as a means of deal with the pressure to meet academic expectations (Vaughan, Corbin, & Fromme, 2009). Alcohol or recreational drugs offer the illusion of relief from some of the stress and anxiety associated with college. Substance use can also contribute to a vicious cycle of substance-related poor academic performance, increased stress, increased use of chemicals to address that stress, and then further deterioration in academic performance. Johnson (2010) reported, for example, that one-quarter of college students admitted that their alcohol use had caused drinking-related academic problems such as missing classes, poor grades, or failing to keep up with assigned materials.

In contrast to the student population with strong academic goals, some undergraduates find that heavy alcohol use facilitates the establishment of social relationships with other heavy alcohol users, and is a strong motivating factor for continued heavy alcohol use. Unfortunately, there is an inverse relationship between the individual's level of alcohol use and academic performance, as many students discover to their dismay⁹ (Vaughan et al., 2009; White & Hingson, 2014). In the next section we will look at the changing relationship between the student, alcohol, and illicit drugs.

An Evolving Relationship

The individual's relationship with alcohol during young adulthood does not remain static. Over the course of their academic careers, some students who were initially most invested in heavy alcohol use have been known to turn their attention to academic studies. This change in priorities might be motivated by the discovery that the student is moving closer to graduation and soon will attempt to enter the workforce (Vaughan et al., 2009). Also, students frequently find

that upon reaching legal adulthood the thrill of drinking is lost: It is no longer a prohibited activity for them.

While in college, students discover that there are rewards for their efforts and that life can also be unfair. Some students find that their initial choice of a field of study no longer holds their interest and discover a passion for another academic pursuit. This change in academic focus¹⁰ potentially can force the student to develop new social networks, possibly establishing social networks with students who are more heavily invested in academic performance rather than alcohol or drug use. The distinctive demands of postsecondary education may conspire to prevent the individual from completing his or her chosen program of study for a variety of social or financial reasons. Some students, faced with overwhelming financial demands, either drop out of school, transfer to institutions where the tuition is more affordable, or elect to pursue part-time studies intermixed with employment to pay for their educational careers. Some students fail to graduate because of illness, accidents, disease, or the unplanned demands of parenthood.¹¹ Each course of action forces the students to establish new social network systems with similar, or different, social relationships and to reexamine their substance use pattern.

One factor that influences the young adult's relationship with alcohol is his or her ethnic heritage. Many Latino and African American students are the first members of their family to attend college, thus introducing the possibility that familial pressures to perform well in the college environment and advance socially following graduation. These are strong factors that might inhibit the use of alcohol by these students (Vaughan et al., 2009). Asian American students often enter college with strong social and familial pressure to succeed in their studies, even if they are not the first members of their family to attend college (Vaughan et al., 2009). In contrast, Caucasian students often bring an expectation that heavy alcohol use is an integral part of the college experience, contributing to alcohol misuse by this population of students (Vaughan et al., 2009). Women in all subgroups tend to be more academically oriented, especially during the early years of college, which tends to protect them from alcohol misuse problems in college (Vaughan et al., 2009).

Hypothetically, the protected college environment might be one reason why college students are more likely to engage in binge drinking, as opposed to their non-college peers. College enrollees were less likely than their peers who are not college-bound to be binge drinkers in high school, a pattern

⁹It is not unusual to discover that those freshmen who were most heavily invested in the "party" scene in the fall semester are either on academic probation during the spring semester or have been dismissed from college for their poor academic performance in the preceding semester. Unfortunately, this phenomenon is not limited to first-year college students.

¹⁰Also known as "switching majors."

¹¹Which itself might be a result of the disinhibition effects of alcohol misuse and high-risk sexual activity encouraged by alcohol's disinhibition effects.

that reverses itself after they enter college. Just over 4% of college students admitted to using alcohol daily, while 5% of their non-college peers admitted to having done so (White & Hingson, 2014). The number of college students who consumed five or more drinks on one occasion (binging) in the previous 30 days remains relatively stable at 44%, despite their non-college peers who engaged in binge drinking in the previous 30 days having dropped from 39% in 2002 to 36% in 2010 (White & Hingson, 2014).

Young adults view beer differently than other forms of alcohol, consuming a greater amount of beer per drinking episode than they would if consuming hard liquor (Bonar et al., 2012; Quinn & Fromme, 2012). This places them at greater risk for adverse consequences from a binge because of the higher blood alcohol level¹² that results from this misperception. Male college students reported that a binge required the consumption of a greater number of drinks than did female students, suggesting that studies on this topic should be gender-specific (Bonar et al., 2012). College students are more likely to drink with the goal of intoxication than their non-college peers. Persons who did not enter college report more frequent alcohol use and are more likely to be individuals who drink daily as compared to their college peers, but tend to drink less per occasion as well (Bonar et al., 2012). This information underscores the differences between these two subgroups of transitional adolescents or young adults.

During the college experience, dating relationships continue to evolve, and the student confronts the possibility of finding a future life partner. Courting rituals might be initiated either to immediately progress to their anticipated goal, or the goal is acknowledged but by agreement is postponed until after graduation. Experimental relationships (heterosexual or homosexual) also evolve during the college years, often to slowly dissolve during or shortly after the college years. However, some relationships that begin in college do continue, and couples who marry after college graduation appear to experience a lower divorce rate (Furstenberg, 2010).

Scope of the Problem

Substance use by college students is hardly a new phenomenon. In 1355, for example, there was a drunken brawl between students of Oxford University in England and the local

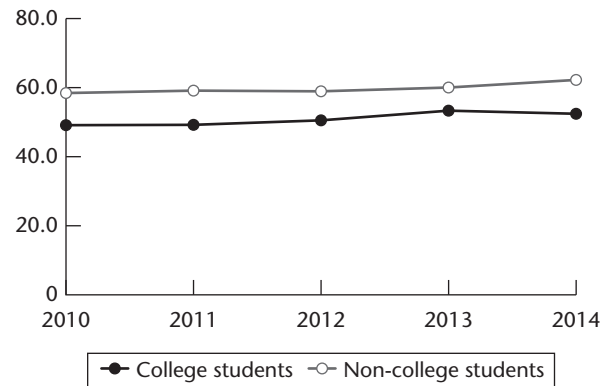


FIGURE 21-1 Percentage of 18–29-Year-Olds Admitting to Substance Use

Note: This figure includes those individuals who report having misused an illicit chemical just once as well as those who use regularly.

SOURCE: Johnston et al. (2015b).

townspeople that left 63 students dead (Boyd, McCabe, & Morales, 2005). Currently, alcohol use remains ubiquitous in the college environment. The start of the “chemical revolution” eventually presented society with a growing number of new compounds that potentially could be misused, a fact to which many students in postsecondary institutions will attest. For example, in rare cases, medical and dental school students have used surgical anesthetic agents such as ether for recreational purposes. However, the average person does not have access to these compounds. Still, adults in the same age group as medical school students do misuse chemicals. Surprisingly, although alcohol misuse is higher in college students, substance misuse seems to be more pervasive in the general population of 18–29-year-olds who do not attend college than college students in the same age group, as illustrated in Figure 21-1.

The use of stimulants to help the student “cram” for final examinations is pervasive, involving between 16 and 30% of the student body at some colleges (Benson, Flory, Humphreys, & Lee, 2015; Frances, 2013). In spite of the stereotype of college students being most likely to misuse CNS stimulants for this reason, 18.7% of non-college adults in the 19–28 age group admit to having used an amphetamine at least once, as opposed to 15.0% college students (Johnston et al., 2015b). Nor do college students neglect such compounds as marijuana, hallucinogens, or other drugs. Mainly people use these compounds out of curiosity; however, some college students go on to make the use of such compounds an informal program of study.

Although it is illegal for students under the age of 21 to drink in most states, just under 90% of college students consume alcohol and view it as a central component of their social life. Approximately 40% of college undergraduates

¹²The team of Goslawski and colleagues (2013) found evidence of microvascular changes in young adult binge drinkers, for example, that they surmised might predate later cardiovascular risk. The study was based on a small number of participants, and thus this study should be replicated using a larger number of young adult binge drinkers to confirm these findings.

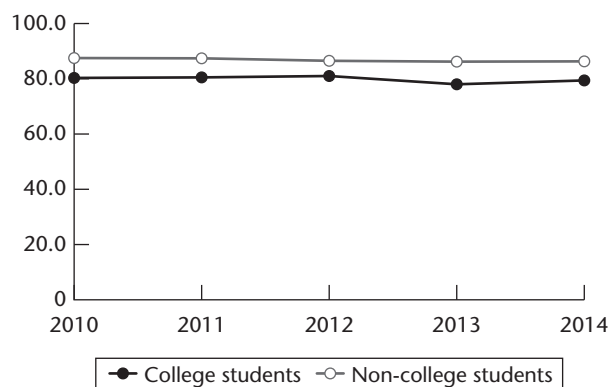


FIGURE 21-2 Percentage of 18–29-Year-Olds Admitting to Alcohol Use During Lifetime

SOURCE: Johnston et al. (2015b).

“engage in heavy episodic drinking at least once every two weeks” (Leeman, Toll, Taylor, & Volpicelli, 2009, p. 553). At many colleges, certain nights are identified as “party” nights, and alcohol use is more common, if not expected, on these nights¹³ (Benton, 2009). Student alcohol use also is very common during special events such as holidays and spring break (Lee, Lewis, & Neighbors, 2009; White & Hingson, 2014), and certain colleges are, in spite of their academic credentials, also known as “party” schools. Students who lived in dormitories were less likely to drive after drinking, possibly because they are less likely to have a car on campus, or their access to a greater number of social activities that do not involve alcohol (Quinn & Fromme, 2012). Figure 21-2 compares the percentage of college students in the 19–28 age bracket admitting to alcohol use at least once as compared with adults in this same age group who did not choose to attend college.

As Figure 21-2 demonstrates, the percentage of 18–29-year-olds who report the use of alcohol at some point in their lives has remained relatively stable for both groups. For college students, certain environments on campus appear to encourage the use of alcohol. The college fraternity offers one notorious environment for alcohol use, although this varies from fraternity (or sorority) to fraternity (or sorority) (Miller, 2013; White & Hingson, 2014). Benton (2009) found that 86% of fraternity members reported binge drinking, a figure that is approximately 35% higher than for college students who are not fraternity members. On a similar note, 80% of sorority members who live in a sorority house report binge drinking, a figure that is approximately twice that for

women who are not sorority members (Benton, 2009). Students often self-select to gain admission to Greek houses with alcohol use patterns more consistent with their level of alcohol intake (Park, Sher, & Krull, 2009).

Lipari and Jean-Francois (2016) combined recent SAMHSA report data and found that 60% of college students had drunk alcohol in the past month,¹⁴ 39% met the criteria for binge drinking,¹⁵ and 13.2% were identified as being heavy drinkers. Although there has been a slight increase in the percentage of college students who engage in binge drinking, this increase was found in the 21–24 age bracket¹⁶ rather than in the 18–21 age group (Hingson, Zha, & Weigznan, 2009). Such binge drinking is, at least in theory, supported by the tradition of “happy hours” at bars near the college campus. There is an initiative by some institutions of higher learning to stop specialized events at local bars that encourage heavy drinking, which have met with mixed results. It has been found, however, that even if such intervention efforts were successful, college drinkers would simply turn to other sources of cheap alcohol and that the frequency of intoxication remains relatively unchanged in this age group (Wells, Graham, & Purcell, 2009).

Certain colleges have reputations as being party schools, and the rate of alcohol use by students at these institutions tends to be higher than at other colleges in the United States. Nelson, Xuan, Lee, Weitzman, and Wechsler (2009) found that 85–88% of students at these colleges engaged in alcohol use, with 53–58% engaging in heavy, episodic alcohol use, percentages that are significantly higher than the national averages for college alcohol use. To combat this problem, there has been an intense effort to curb alcohol use at the 18 colleges with the highest rate of alcohol use, but so far, the percentage of students reporting alcohol appears to have remained stable (Nelson et al., 2009). Further, within the college environment there is a self-selection process through which students seek admission to specialized microenvironments (smoking-permitted vs. smoking-prohibited dormitory units, for example) or off-campus drinking establishments.¹⁷ The known relationship between cigarette smoking and alcohol use would suggest that smoking-permitted dormitory units are more attractive to individuals who smoke as well as individuals who drink, encouraging the incoming student to seek admission to these housing units.

¹⁴The data summarized before this was based on *lifetime* alcohol use, while this study is based on *current* alcohol use.

¹⁵Defined as consumption of five 12-ounce cans of beer, or standard mixed drinks, in a period of drinking.

¹⁶Student age group for returning students or graduate school students.

¹⁷A small number of colleges and universities do allow the sale of alcohol in designated areas.

¹³Which for some college students begins on Thursday night, depending on their class schedule.

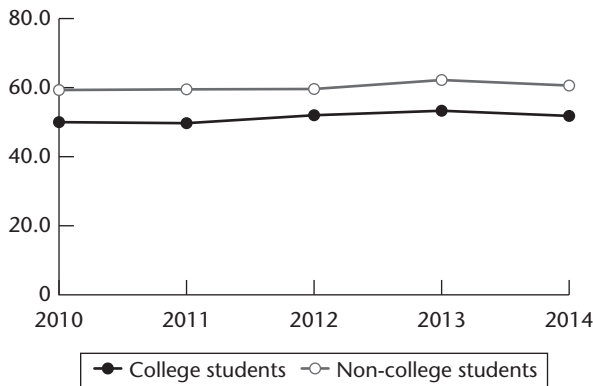


FIGURE 21-3 Percentage of 18–29-Year-Olds Admitting to Illicit Drug Use at Least Once During Lifetime

SOURCE: Johnston et al. (2015b).

One interesting apparent in Figure 21-1 is that the percentage of 18–29-year-olds who did not attend college is higher than the percentage of students in the same age cohort who attended college. This reflects the tendency for non-college adults to indulge in limited alcohol use at the end of the workday, as opposed to college students who are more likely to engage in binge drinking on limited occasions¹⁸ and abstain from alcohol use during the week. The percentage of individuals in the two 18–29 age cohorts who report having misused an illicit drug at some point in their lives remained relatively from 2008 to 2014, although there were again intergroup differences in the level of reported substance use, as is seen in Figure 21-3.

The most commonly misused drug for both groups is marijuana, although other compounds such as narcotic analgesics that have been diverted for illicit use appear to be a growing problem (Johnston et al., 2015b). Lipari and Jean-Francois (2016) found that 6% of full-time college students used illicit drugs for the first time in the past year, compared to 3.8% of part-time college students. The similarity in substance use patterns for college versus non-college students is perhaps best illustrated by the fact that 5.0% of college students reporting having used MDMA in the previous year, as opposed to 4.8% of their non-college peers (Johnston et al., 2015b). More than 34% of college students in the 18–29 age cohort admitted to the use of marijuana at least once in the previous 12 months, as opposed to 31.6% of their non-college counterparts (Johnston et al., 2015b). Yet another example of the similarity of the two subgroups is found in the fact

that 4.0% of college students admitted to the use of a hallucinogen at least once in the previous 12 months, as opposed to 4.1% of the non-college members of the 18–29-year-olds sampled.

There is an interesting difference between college students and their non-college peers in the reported level of cigarette smoking. Johnston and colleagues (2015b) found that 22.6% of the 18–29-year-old college age bracket admitted to the use of cigarettes at some point in their lives, but 27.0% of non-college students admitted to the use of cigarettes at some point.

One frequently overlooked aspect of college students with SUDs is those students who utilize a performance-enhancing compound such as anabolic steroids, CNS stimulants, and nutritional supplements. Buckman, Yusko, White, and Pandina (2009) examined this student subpopulation and found that those who used performance-enhancing compounds tend to demonstrate problematic alcohol use, are more likely to smoke cigarettes, are more likely to use cocaine, marijuana, and hallucinogens, and are more likely to misuse prescription drugs.

Group Insulation

College students tend to *overestimate* their peers' acceptance of drunken behavior, and they overestimate the number of their peers who are engaging in heavy alcohol use, both factors that contribute to abnormal alcohol use patterns by college students (Park et al., 2009; White & Hingson, 2014). College students also overestimate the frequency with which their peers suffer negative consequences from their drinking, and often mistakenly believe that such negative consequences of alcohol use are the norm for their age cohort (Lee, Geisner, Patrick, & Neighbors, 2010). Often this reduces the power of alcohol-related adverse consequences to inhibit further alcohol use. Further, there is a relationship between the student's living environment and his or her alcohol use level. College students experience a closed environment, or what is known as "group insulation" (Neighbors, Pedersen, & Roberts, 2009, p. 14). As a result of this process, they are protected against all but the most severe repercussions of their alcohol use (Neighbors et al., 2009). This process tends to isolate college students from external influences on their behavior, especially alcohol use. External norms are often ignored, classified as irrelevant, or discounted in favor of continued alcohol use (Neighbors et al., 2009). In the next section, we will examine some of the more common problems encountered by the individual who has problems with drinking or using drugs during the college years.

¹⁸Such as the blue-collar worker who has one to three beers at the end of the workday, as opposed to the college student who goes out with friends to drink on the weekend, but who abstains during the week.

Consequences of Substance Use Disorders in the College Population

The individual's response to a drug of misuse will be influenced by his or her central nervous system's level of maturation, and, in spite of protests to the contrary, the brain of the typical 18–21-year-old is still developmentally immature (Jorgensen, 2008). For example, the adolescent brain is four to five times more vulnerable to alcohol-induced brain damage than the fully mature adult brain (Tapert, Caldwell, & Burke, 2004/2005; Wuethrich, 2001). This accounts for the paradox that in the young adult population those who drink at a light or moderate level outnumber those who drink heavily, but paradoxically are responsible for the greatest number of alcohol-related problems. Adolescents who drink show a small (7–10%) decline in psychological test performance as compared to their nondrinking compatriots (Strauch, 2003). Alcohol misuse has also been found to damage the **hippocampus**¹⁹ in the brain in college-aged adults, suggesting one reason why alcohol misuse by college students or young adults might have lifelong consequences. The frontal lobes have not become fully integrated into the brain's structure in this age group, and have not fully assumed their duties in assessing and planning behaviors; it is not known whether alcohol use or misuse in the 18–29 age group affects this process (De Bellis et al., 2000; Tapert et al., 2004/2005).

Paradoxically, the developmental immaturity of the student's brain during the early adult or college years might *predispose* individuals to alcohol's reinforcement (Spear, 2002). Heavy alcohol use has been identified as one factor that appears to facilitate the development of a compound known as **C-reactive protein**²⁰ in the body (Bell, Mehta, Moore, & Britton, 2017). This compound is thought to be associated with the development of heart disease (Bell et al., 2017; Gupta, 2007). The research thus far supports the idea that previous heavy alcohol use continues to impact the development of this protein for at least a decade (Bell et al., 2017), and thus the individual's use of alcohol during the college years might have lifelong consequences for the drinker. Fortunately, only a minority of college students appear to continue to drink abusively after graduation, which may limit the alcohol-induced production of C-reactive protein following graduation.

Binge Drinking

As was indicated earlier in this chapter, college students engage in more binge drinking than their non-college

peers. Lamentably, even binge drinking is not without its dangers. An emerging body of evidence suggests that binge drinking can contribute to neurological dysfunction. Crego and colleagues (2009) identified a sample of college students who engaged in binge drinking, and administered a battery of neuropsychological tests. The authors found that although the binge drinkers were able to complete the subtest tasks, they required higher levels of attentional effort to do so compared with their nondrinking peers. The authors interpreted this as evidence that even binge drinking might result in subtle neurological deficits.

One area of special concern is the tradition in which the college student celebrates his or her 21st birthday with the consumption of alcohol. Between 80 and 90% of college students consume alcohol to help them celebrate upon achieving this milestone (Day-Cameron, Muse, Hauenstein, Simmons, & Correia, 2009). This landmark is often marked by drinking rituals, many of which are sponsored or at least encouraged by peer expectations and the drinking establishments near the campus. Many drinking establishments provide the birthday celebrant with free alcohol or alcohol at a markedly reduced rate (Brister, Sher, & Fromme, 2011).

The consumption of 21 drinks by the student on their 21st birthday is fortunately uncommon (2% of cases reviewed). However, the expectation that these students do so within an hour's time is not uncommon, in part because the student or young adult feels the need to prove that they are able to accomplish this task in spite of potential consequences. By following this practice, the student plays a "chemical equivalent of Russian roulette" (Neighbors et al., 2009, p. 14). The outcome is often the need for emergency hospitalization for acute alcohol poisoning or, in some cases, the student's death.

Indirectly, the practice of celebrating one's 21st birthday with alcohol can lower inhibitions, which in turn can contribute to the individual's decision to engage in high-risk behaviors such as unprotected sex or driving while under the influence of an intoxicant (Brister et al., 2011). Undergraduate women who drank to the point of intoxication at an earlier age, and who engaged in heavier alcohol use in the 3 months before they officially turned 21, were all predictors of birthday drinking, according to the authors. Peer group influences were an important part of the student's decision to drink to celebrate their 21st birthday, as were the individual's expectations for both the alcohol and the celebration. Peer pressure to drive after drinking also contributes to the increased risk for arrest for driving while under the influence of an intoxicant (Quinn & Fromme, 2012).

¹⁹See Glossary.

²⁰See Glossary.

Energy Drinks

Approximately one-quarter of college student drinkers believe the myth that they can mitigate the effects of their alcohol use by interspersing periods of drinking with the ingestion of “energy drinks” (Spear, 2010). To explore whether this belief was true or not Thombs and colleagues (2010) obtained blood alcohol levels from 802 college students who were selected at random as they exited a bar at the end of the night. They found that those students who had consumed energy drinks were 300% more likely to leave the bar highly intoxicated, and 400% more likely to plan to drive home than were those students who did not consume energy drinks that evening. Thus, rather than mitigating the effects of the alcohol consumed, such behavior appears to encourage the over-use of alcohol, with the concomitant dangers associated with excessive alcohol use.

CNS Stimulants

The misuse of central nervous system stimulants such as the amphetamine compounds or Provigil® (generic name: modafinil) is rampant at some institutions of higher learning, with as many as 30% of the students using a CNS stimulant(s) to help them “cram” for examinations at some point in their academic career (Frances, 2013). Medication diversion is the most common means by which students obtain these medications, which they use on the basis of the unsupported assumption that the medications will help them improve performance on examinations (Arria et al., 2017). In contrast, just 1% of adults in the 19–20 age cohort in the general population admitted to using methamphetamine at some point in their lifetime, and 0.4% of adults in the designated age bracket who admit to the unauthorized use of modafinil (Johnston et al., 2015b). The earlier statement that college is a unique environment is underscored by these drastic differences, and they illustrate how CNS stimulant misuse is a very real problem at many institutions of higher learning.

Tobacco Use

There is an interesting relationship between educational levels and use of tobacco products. An estimated 24% of young adults who did not graduate from high school smoke cigarettes, as opposed to 18% of individuals with some college experience and 7% of college graduates (Centers for Disease Control and Prevention, 2016). Surprisingly, many college students begin to use tobacco products while in college, either for the stimulant effect of the nicotine to help them stay up to study longer, or to drink

more alcohol, or for its anorexic effect to help them control their weight. These students risk any of the adverse consequences of tobacco use or tobacco use disorder outlined in Chapter 15.

Illicit Drug Use

It is the misuse of illicit substances that carries the most significant list of potential legal consequences for college students: The acquisition and possession of illegal substances are grounds for legal sanctions, which might include incarceration and loss of access to financial assistance programs for the student. Additionally, use of illicit drugs has been linked to an increase in risky sexual behavior, sexual aggression, and regretted sexual behavior in college students (Parks, Frone, Muraven, & Boyd, 2017). Additionally, there can be a number of other consequences, including negative psychological impact, sleep disturbances, physical impact, etc., as discussed in previous chapters in this text, in addition to the potential for negative impacts on students' grades and overall GPA (Parks et al., 2017).

Intervention

Intervention programs for college students who misuse or are addicted to chemicals are still in their infancy. Bhochhibboya, Hayes, Branscum, and Taylor (2015) performed a review of the professional literature and found just 14 journal articles that addressed this problem. They found that, in spite of the different methodologies utilized in these different studies, 13 of the 14 studies demonstrated a reduction in chemical use (usually alcohol) by the college students involved. Unfortunately, students whose behaviors suggest that the individual might have an SUD are referred to off-campus rehabilitation professionals or self-help groups. There is virtually no data available to suggest what percentage of these students actually participated in the rehabilitation programs suggested or the success rates of these referrals. However, today's college student population grew up in the electronic era and feel quite comfortable using computers or cell phones. Drawing upon this social phenomenon, Bhochhibboya et al. (2015) developed an internet-based brief intervention program that appeared to be more effective than face-to-face programs. Other electronics-based programs are also being developed and tested, including gamified and Facebook-connected applications that have gained initial research support (Boyle, Earle, LaBrie, & Smith, 2017). Ultimately, access to intervention and other services is the key (Leebens & Williamson, 2017), which may mean continued development of online and app-based intervention programs.

Post-Graduation and Graduate School

Graduate studies are a prerequisite for entry into some professions, such as the law, psychology, and medicine.²¹ For some students, graduate school is simply a way to escape from the responsibilities of adulthood for a few more years (Benton, 2009). For both groups, substance use and misuse are potential problems. Some individuals continue the substance use pattern(s) established during their undergraduate program. However, the majority of graduate students begin to “mature out” of the substance use patterns established in their undergraduate years. Surprisingly, former undergraduate students²² turn to their parents’ substance use beliefs and behaviors for guidance, especially in the first two to three years following graduation (Boyd, Corbin, & Fromme, 2014). During that time, they are also actively establishing a new social support system whose substance use beliefs and behaviors are more consistent with their own evolving attitudes toward substance use (Boyd et al., 2014).

Unfortunately for some professionals-in-training, heavy alcohol use in social settings allows for professional “networking” in which opportunities for both clerkships and summer study programs might be discussed, and where the foundation for later professional relationships might be established. Alcohol use during these competitive graduate programs also provides students with a chance to “decompress,” often with surprising results. A survey of medical school students found, for example, that 11% drank excessively, while 18% met the criteria for a diagnosis of a mild AUD (Benton, 2009). Surprisingly, these students appeared to perform better academically than their nondrinking peers (Benton, 2009).

Following graduation, students discover two inconvenient realities: First, the sheltered environment of college does little to prepare the individual for the hustle and demands of the work environment. The department supervisor does not care whether you had competing deadlines for different projects: He or she will want assigned projects completed on time, and within budget. Students might receive an extension for a term paper that was not quite finished, for example, but that individual would be quite unlikely to get an extension on work assigned after graduation. Second, students often discover with some degree of shock that the career they prepared for, and in which they invested a significant portion of their life and financial resources, might not be the panacea that they had hoped for (Benton, 2009).

To help them face the demands of their work career in the face of these discoveries, most former students either modify or discontinue their use or misuse of chemicals. Personal expectations are adjusted, and career goals are either modified or possibly dropped entirely. For a minority of graduate school students, alcohol or the other drugs used during college and graduate school might serve as an “anchor” during this transition period (Benton, 2009). Alcohol consumed during graduate school will have the same effect as alcohol consumed while in the workplace, providing a familiarity and predictability, not to mention escape from bruised emotions, that provides a strong incentive for the person to continue to misuse alcohol or other chemicals. Further, if heavy alcohol or drug use was the expectation during the decompression and networking periods after the week’s studies, former students might carry these expectations with them into the work environment, with potential psychosocial, vocational, and legal problems resulting from their chemical use. Unfortunately, there is evidence suggesting that upscale men’s clothing stores are using alcohol as a possible way to entice customers (Dokoupil, 2009), adding to the allure of alcohol during what is for many young adults a difficult transition.

Are There Forces That Help Protect the Student from SUDs?

The answer to this question is an unqualified “yes.” College students share the same risk factors and protective mechanisms that are found in the general population. Active religious involvement, for example, has been found to reduce the student’s risk for developing an alcohol use disorder by 40% (Lambert, Fincham, Marks, & Stillman, 2010). Peer group affiliation and personal goals and aspirations might both be viewed as protective factors. Strong interpersonal ties provide assistance in maintaining resilience in the face of adversity (Leebens & Williamson, 2017; Southwick & Charney, 2013). Parental influence, while not as strong as during the childhood and adolescent years, still can help to shape the student’s substance use pattern. Role models also help to shape the student’s substance use behaviors, and finally an often-overlooked factor that occasionally helps to protect the student from developing a substance use disorder is plain old common sense. This list is not all-encompassing (sibling feedback was not mentioned as a protective factor, for example), but it does illustrate that there are individual-specific protective forces that assist the transitional adolescent in avoiding the pitfalls of a substance use disorder.

Other factors that help to limit the misuse of alcohol by college students are the scheduling of classes on Fridays, with frequent quizzes being administered on these days

²¹Medical school might be viewed as a form of graduate school.

²²A term which here is applied to those students who have graduated from a 4-year institution, whether they go on to graduate school or not.

(Saitz, 2011). This discourages the student from using alcohol on Thursday evenings, which is often considered a party night on many campuses. Other systemic interventions have been implemented, such as increasing the tax on alcohol, raising the minimum drinking age to 21, and rigid enforcement of laws against driving under the influence of alcohol (Saitz, 2011).

Chapter Summary

The period of late adolescence or young adulthood presents a conundrum: Is the individual an adolescent or a young adult? To solve this question, it is suggested that the individual be viewed as a transitional adolescent, a person who is legally defined as an adult and who presents personality traits normally seen in young adults as well as other traits more traditionally seen in adolescents. During

this phase of transition, individuals are faced with a number of choices that will influence the rest of their lives. One such decision is whether to pursue a college degree in the hopes of enhanced earning potential later in life, or to enter the workforce immediately. Slightly under half of persons in the 18–19 age cohort do enter an institution of higher learning. In many cases, the individual does not complete more than a semester or two before dropping out of school because of financial, social, or familial factors that prohibit further participation in higher education. The individual's relationship with alcohol and illicit drugs is transformed now that they are in the earliest stages of adulthood, with different implications for those who choose to enter an institution of higher education as opposed to those transitional adolescents who do not follow this path. In this chapter, some of these differences were discussed.

Substance Use Disorders and the Older Adult^{1,2}

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 22.1** Understand the scope of the problem of substance use and misuse in older adults
- 22.2** Understand the consequences of SUDs for older adults
- 22.3** Consider the challenges in detecting SUDs in older adults
- 22.4** Review the treatment of SUDs in older adults

Introduction

It was once thought for that substance use disorders (SUDs) were self-limiting. The negative health consequences of substance misuse were thought to prevent the majority of older drinkers from achieving their normal anticipated lifespan (Brennan, Schutte, & Moos, 2010).³ There also was (and in many places remains) a popular misconception that older persons do not misuse drugs, and so health care professionals do not need to worry about the SUDs in this subpopulation. These misperceptions might be a result of the fact that physicians usually lack the training and skills to diagnose SUDs in older individuals (De Jong et al., 2016; Klimstra & Mahgoub, 2010; Oslin & Zanjani, 2016; Zimberg, 2005) and thus generally do not screen for substance misuse in older persons (De Jong et al., 2016; Ellison, 2012).

¹In past editions of this text, the topic of substance use disorders in older age cohorts was included as a part of a separate chapter. However, as the “baby boomer” generation ages, it has been found that they continue to misuse chemicals, and a wider variety of chemicals, than earlier elderly age groups. For this reason, this topic is now the subject of a separate chapter.

²Defined, for the sake of this text, as post-retirement age, or after the age of 65, although some studies use a cut-off age of 50. Thus, there is some confusion among researchers about how “elderly” might be defined. For the sake of this text, the term *older individual* will be used to identify persons over 60 years of age.

³Although research data *does* suggest that older drinkers consume less alcohol than their younger counterparts, this might be an illusion caused by the fact that because of age-related changes in their bodies they do not *need* to drink as much to achieve the same effect as they did when they were younger.

Scope of the Problem

The age cohort born between 1945 and 1965 (or 1946 and 1964 per some sources), the so-called “baby boomers,” came of age in the 1970s and 1980s, when there was a more permissive social attitude that tolerated substance use (Colliver, Compton, Gfroerer, & Condon, 2006; Drew, Wilkins, & Trevisan, 2010; Ellison, 2012; Wang & Andrade, 2013; Zimberg, 2005). Around 75 million individuals in this age group are about to or have reached retirement age. By 2029, more than one-fifth of the population of the United States will be 65 or older (Colby & Ortman, 2014). Globally, there is an expected 1 billion increase in the number of people in this age group by 2050 (Wu & Blazer, 2014), with those over 60 outnumbering those under age 5 by 2020 (World Health Organization, 2015). An individual’s entry into the early stages of older adulthood does not automatically mean that he or she will alter earlier substance use patterns. Many bring an established substance use disorder with them as they enter the stages of older adulthood. Wang and Andrade (2013) suggested that 2% of persons in the United States over the age of 50 admitted to the use of an illicit drug in the past 12 months. Also, many “baby boomers” develop an SUD after they reach the age of 65 as a result of social isolation, age-related illness, and the loss of purpose that often accompanies retirement. Alcohol is the compound most commonly misused by older adults; however, 15% of older individuals who drink also have a concurrent drug use disorder (Ellison, 2012; Greenfield, 2007). Collectively, alcohol or substance misuse either is or will be a problem for at least 19% of those over the age of 65 (Blazer & Wu, 2009; Blow, Serras, & Barry, 2007; Wu & Blazer, 2014), with AUDs being the third most common psychiatric problem found in older people (Luggen, 2006).

Marijuana use continues to be common in the baby boomer generation, with the rates of use increasing over the past decades in older adults (Hasin et al., 2015). Marijuana in the 55 and older age bracket was the most commonly used illicit compound (“Illicit drug use among older adults,” 2009). In the United States, 11.4% of those individuals in the 50–64 age group reported having used marijuana just in the past 12 months (Fahmy, Hatch, Hotopf, & Stewart, 2012; Shadel & Scharf, 2012). An additional 11% admitted to the use of another illicit drug in the past 12 months (Shadel & Scharf, 2012). According to recent NSDUH data, the greatest increase for use within the past month was for those 55 and older (Azofeifa et al., 2016).

Marijuana use in middle or older adulthood can cause or exacerbate memory impairment, itself a significant complaint for older adults (Auer et al., 2016). It is not known at this time whether marijuana cessation will reverse part or

all of this substance-exacerbated memory impairment. The misuse of psychoactive prescription drugs is an unexplored area of concern for individuals over the age of 65 (Wang & Andrade, 2013). The percentage of adults over the age of 50 who are thought to misuse prescribed medications is thought to have increased from 2.2% in 2002 to 3.9% in 2009, with analgesics being the most common category of misused pharmaceuticals, followed by anxiolytics, and then hypnotics (Wu & Blazer, 2011). Horstman (2010) also suggested that older individuals who continue to work in this age group are using CNS stimulants such as methylphenidate or an amphetamine to help them compete with younger, more energetic and intellectually more creative coworkers.

Almost half of men and slightly over one-third of the women over the age of 60 use alcohol (Barnes et al., 2010), and the greatest proportion of those who use alcohol are social drinkers. Drawing upon data from the English Longitudinal Survey on Aging, Iparraguirre (2015) found that retirement was a risk factor for increased alcohol use in women over 50, but not for men. Not surprisingly, caregiving responsibilities reduced the probability of alcohol use disorders for women over 50, according to the author. Higher educational levels and tobacco use were associated with an increased probability of harmful alcohol use for both sexes. Men who were single, separated, or divorced were at increased risk for harmful drinking, according to the author, who also reported that men who enjoyed higher income levels were also at risk for harmful drinking. It is not known at this time whether older drinkers in the United States follow this pattern, but this is not an unreasonable assumption until research disproves this theory.

Because of age-related physical changes, health problems, and the concurrent use of over-the-counter and prescribed medications, even moderate alcohol use⁴ carries the potential for negative consequences in the older drinker (Barnes et al., 2010; Ellison, 2012; Kalapatapu, Paris, & Neugroschl, 2010; Klimstra & Mahgoub, 2010). Because of age-related physical changes, the level of “moderate” alcohol consumption in those who are over 65 is now defined as just one standard drink or can of beer in a 24-hour period, and hazardous alcohol use is now defined as more than three drinks in one sitting, or more than seven drinks in a 7-day period (Drew et al., 2010; Wang & Andrade, 2013). Note that these guidelines are related to healthy adults over age 65 who do not take any medications.

⁴Defined, as you will recall, as one to two standard drinks for a man, and one standard drink for a woman.

What Are the Consequences of an SUD in the Older Adult?

As a group, the older adult population uses one-third of prescription medications and one-half of all over-the-counter medications sold each year in the United States (Gross, 2008; “U.S. face of drug abuse grows older,” 2006). Unfortunately, many of the more popular drugs that are misused, including alcohol, can interact with pharmaceuticals used to treat many diseases, increasing the potential for a harmful alcohol–medication interaction. More than 75% of those over 65 who take a medication that interacts with alcohol continue to acknowledge drinking (Castle, Dong, Haughwout, & White, 2016), and at least 19% of older individuals who drink alcohol will experience at least one adverse alcohol–drug interaction (Brust, 2004). Around 28% of all hospital visits involving adverse alcohol–drug interactions are within the age group of 55 and older, with over 50% of those visits involving alcohol and central nervous system drugs (Castle et al., 2016). If the individual were to also have an SUD, the risk of an adverse drug–drug interaction is multiplied, possibly with fatal results (Gwinnell & Adamec, 2006; Stevenson, 2005; Zimbert, 2005).

The misuse of alcohol or other illicit substances can also exacerbate many medical disorders, adding to the tendency for this age group to use health care resources more often than younger people (Stevenson, 2005). The side effects of many of the compounds being used simulate, or at least exacerbate, medical or psychiatric disorders in this age cohort. It has been found that older persons with an AUD are also at increased risk for depression, memory problems, liver disease, cardiovascular disorders, and sleep problems (Luggen, 2006; Rigler, 2000; Zisserman & Oslin, 2004). Because age-related decline in reaction time is compounded by the effects of various compounds of misuse,⁵ older people with an SUD are also at increased risk for motor vehicle accidents.

Older people with an SUD are known to be at increased risk for dementia or pseudo-dementia caused or exacerbated by the vitamin absorption deficiencies often seen in people with substance use disorders. Just the alcohol use disorders in older people can cause or exacerbate myopathy, cerebrovascular disease, gastritis, diarrhea, pancreatitis, cardiomyopathy, cirrhosis, hypertension, diminished immune response to infections, peripheral muscle weakness, electrolyte and metabolic disturbances, depression, and hypotension. Confusion (rather than a tremor) might be the most prominent sign of

alcohol withdrawal in older individuals who drink heavily, and the person’s visual and/or tactile hallucinations during withdrawal might persist for weeks or months after stopping alcohol consumption (Klimstra & Mahgoub, 2010).

Depression is a common problem in older adults, in part because of the vitamin malabsorption syndromes that develop with age, or a prior alcohol use disorder. Other possible reasons for depression in this age group include lack of income, housing, and living alone. The person who is depressed is at increased risk for suicide, and it has been estimated that 25–50% of all older people who attempt suicide have used alcohol before their attempt to take their own lives. If the individual’s SUD is not recognized, then the depression cannot be appropriately treated, increasing the person’s risk for a suicide attempt.

Even limited use of cocaine, opioids, or amphetamines carries with it an increased risk of premature death for the older adult from accidents, medication–drug interactions, depression, strokes, or possibly an overdose (Kertesz et al., 2012). Although intuitively one would expect that drug overdoses would be most commonly found in the young adult population, one study of 3,700 drug-related deaths in California found that only 51 involved victims under the age of 20, and that more than half were between the ages of 35 and 54 years, and the remainder involved older adults (Sherer, 2006). There are several possible reasons for these overdoses: First, age-related changes in the body make the individual more vulnerable to the negative effects of alcohol and other drugs (Drew et al., 2010; Klimstra & Mahgoub, 2010; Stevenson, 2005). For example, by the age of 65 cerebral blood flow has decreased by 15–20% (Ellison, 2012). There is also an increase in total body fat levels, while lean muscle mass decreases with the passage of time (Ellison, 2012). While researchers have identified older adults as being at higher risk for suicide, the relationship between higher risk for suicide in this age group and substance misuse is more tenuous and should be interpreted with caution.

Why Is the Detection of SUDs in Older Adults So Difficult?

There are several reasons for this problem. First, there were until recently no screening tools for drug misuse designed and/or validated for use with older adults (Bommersbach, Lapid, Rummins, & Morse, 2015; Klimstra & Mahgoub, 2010). Although there are current screening tools that can be utilized, such as the Screening, Brief Intervention, and Referral to Treatment (SBIRT) tool as well as the Florida Brief Intervention and Treatment for Elders (BRITE) (Schonfeld et al., 2010), additional tools are needed to cover

⁵This increased reaction time might also be caused by many prescribed medications.

more settings and issues (Sorrell, 2017). Also, older individuals tend to have more medical problems than do younger persons; in the earlier stages, the SUDs often mimic the symptoms of many other disorders, making the differential diagnosis difficult for the physician who might be unaware of the patient's substance use status (De Jong et al., 2016; Drew et al., 2010; Stevenson, 2005). This problem is exacerbated by the fact that many older adults who misuse substances attribute these symptoms to physical illness rather than their substance use (Drew et al., 2010), turning for assistance toward physicians who rarely recognize SUDs in this population. Some health care workers might also believe that older individuals *deserve* to use alcohol (or, less often, illicit drugs) as a reward for a lifetime of hard work (Stevenson, 2005; Zimberg, 2005).

Social isolation might also make it difficult for some individuals with an SUD to be identified, especially if the person is a “closet” drinker or drug user. For socially active older drinkers, their friendship circle might contribute to pressure to continue drinking well into their later adult years (Brennan et al., 2010). Further, older people with an SUD will rarely demonstrate the traditional warning signs of an addiction such as the substance-related legal, social, or occupational problems found in younger adults misusing substances (Drew et al., 2010; Klimstra & Mahgoub, 2010). If an older person with an SUD who is in the workforce should miss work because of an SUD-related problem, it is easily explained away as an age-related problem, or as caretaking for a sick spouse. Also, if a person should suspect that an older family member has a substance use disorder, familial shame might demand that the issue remains hidden.

Different Patterns of Alcohol/Drug Misuse in the Older Adult

Kalapatapu and colleagues (2010) suggested that alcohol use in older adults falls on a continuum:

Abstainer: Drinks less than one or two drinks in the previous year.

Social drinker: Drinks no more than one drink per day, and does not show symptoms of an alcohol use disorder.

At-risk drinker: Drinks more than recommended amounts but with few health or social consequences.

Abusive drinker: Drinks above recommended amounts, and has experienced medical, psychological, or social consequences from drinking.

Dependent drinker: Preoccupation with alcohol, loss of control over alcohol use, continued use in spite of adverse social and physical consequences, as well as physical dependence on alcohol.

Of these five categories, the authors suggested that the majority of older individuals fall in the first category. Another classification of older adults who misuse alcohol was offered by Klimstra and Mahgoub (2010). The first subgroup consists of those individuals who did not show evidence of an AUD in young or middle adulthood but who did develop an AUD in late adulthood. These individuals are said to have **late-onset alcoholism** (Klimstra & Mahgoub, 2010; Mundle, 2000; Rigler, 2000). A second subgroup of older adults with AUDs are those people who had intermittent problems with alcohol in young and middle adulthood, but who developed a habitual pattern of alcohol misuse in late adulthood. This subgroup is called the **late-onset exacerbation** subgroup (Klimstra & Mahgoub, 2010; Zimberg, 1995, 1996). Finally, there are those individuals who had problems with alcohol in young adulthood, which continued through middle adulthood into the late adult years, a pattern known as **early-onset alcoholism** (Mundle, 2000; Zimberg, 2005). This subgroup makes up two-thirds of the older population with AUDs (Stevenson, 2005).

Older individuals with early-onset alcoholism were found to come from lower socioeconomic levels, have less formal education, smoke more, socialize with other individuals who misuse alcohol more often, come from families where alcohol use was tolerated or encouraged, be single or divorced, and to more often come from estranged families (Stevenson, 2005). In contrast, individuals with late-onset alcoholism tend to report more adverse life events such as retirement, illness or death of their spouse, loss of lifelong friends, deterioration in health, and depression (Stevenson, 2005). Surprisingly, negative health status does not appear to motivate the individual misusing alcohol to reduce his or her level of alcohol consumption (Brennan et al., 2010).

Prescription Drug Misuse

Prescription drug misuse is often overlooked in older adults by health care professionals, although research has revealed that 20% take medications that are not currently prescribed for them (Barclay, Wright, & Hinkin, 2010). The research to date is challenging to draw conclusions from, given the heterogeneity of the studies, yet it is clear that prescription drug misuse is a growing issue (Maree, Marcum, Saghaei, Weiner, & Karp, 2016). Drug misuse in older age cohorts can take several forms, including (1) mixture of alcohol and

prescribed medications; (2) intentional over-use of a prescribed compound; (3) intentional under-use of a prescribed medication, often to extend the duration between refills; (4) erratic use of a prescribed medication; or (5) failure of the attending physician to obtain a complete drug history, including the use of over-the-counter medications, resulting in dangerous combinations of various compounds (Barclay et al., 2010). In one study, 95% of participants were found to have at least one instance of potential misuse of over-the-counter medications (Stone et al., 2017). Surprisingly, underutilization of prescribed medications is the most common form of medication misuse, usually reflecting the patient's inability to afford the medication (Barclay et al., 2010; Piette, Heisler, & Wagner, 2004).

Twelve percent of persons over the age of 65 are taking at least one benzodiazepine (Ellison, 2012). This class of medications presents a special danger for older users: They increase the individual's risk of falling and suffering a fractured hip by 50%, for example (Klimstra & Mahgoub, 2010). The benzodiazepines also exacerbate the symptoms of dementia, and abrupt benzodiazepine withdrawal can result in disorientation and confusion for the patient. These are symptoms that are frequently interpreted by health care professionals as signs of dementia rather than effects of benzodiazepines on older patients (Klimstra & Mahgoub, 2010). Benzodiazepines that require oxidation as part of the biotransformation/elimination process are not recommended for older patients or for persons with liver disease, as the drug or metabolites might accumulate in the bodies of these users, causing extended problems (Virani, Bezchlibnyk-Butler, & Jeffries, 2009).

The Treatment of Older Patients with SUDs

The number of older persons seeking admission to treatment for SUDs continues to increase, with the number more than doubling between 1992 and 2008 (Treatment Episode Data Set, 2010), and rising from 20% of all admissions in 2004 to 26% by 2014 (SAMHSA, Center for Behavioral Health Statistics and Quality, 2016). Older individuals (defined in this study as people between the ages of 50 and 74) who misuse alcohol are more likely to misjudge their level of impairment at low to moderate levels of intoxication than younger adults (Gilbertson, Ceballos, Prather, & Nixon, 2009). While younger adults are more likely to be polydrug users, older adults were more likely to have just an AUD (Gross, 2008). This pattern is slowly changing as individuals who use multiple substances become part of the older age cohorts.

For many years, there were few outcome studies that focused on older patients with an SUD (Satre, Mertens, Arean, & Weisner, 2004; Zimberg, 2005). Even now, there is a need for continued research to understand the treatment of addictions in older adults (Hassell, Wilkins, & Trevisan, 2017). Even when the older patient with an SUD is referred to treatment, there are few specialized programs that can meet the unique needs of these individuals. These special needs can include (1) a primary prevention program to warn the individual of the potential dangers of alcohol or drug misuse; (2) an *outreach* component to identify and help serve older patients who might be overlooked by traditional social service agencies; (3) *detoxification* programs designed to meet the needs of the older patient with an SUD (who may require longer-than-normal periods to complete the detoxification process); (4) *protective environments* for older patients, including the treatment program setting; (5) *primary treatment* for those people whose status would allow them to benefit from such treatment programs; and (6) *aftercare* programs for older individuals. Ancillary services might include employment services and social work support to help the individual find employment and housing. All of the above would be in addition to long-term residential care for people who have suffered medical or psychiatric damage from their SUDs.

Given the current status of insurance and managed care in the United States, it is unlikely that such extended treatment programs might be developed. However, the need is there: The detoxification process, which in younger adults might be completed in 3–7 days, might require 28 days or more for the older adult with an SUD to complete (Gomberg, 2004; Mundle, 2004; Stevenson, 2005). Even if the older patient does complete the detoxification process, they will often present treatment staff with a range of sensory deficits not seen in young adult patients, and they often dislike the profanity commonly used by younger adults to express themselves. Unless these special needs are addressed, older patients with an SUD are unlikely to be motivated to remain in treatment, or might resist a referral to treatment following relapse (Zimberg, 2005). It is imperative for treatment program staff to be aware of the age-specific stressors that an older person will present when they are in a rehabilitation center setting, such as bereavement, loneliness, and the effects of physical illness (Zimberg, 1996, 2005). On a positive note, there is evidence that older adults with a substance use disorder respond better to an age-specific treatment program than do younger individuals with SUDs (Drew et al., 2010). Older patients were found to remain in primary treatment longer, and to respond to psychosocial interventions such as Alcoholics Anonymous with more enthusiasm, while presenting a lower risk of relapse than seen with other subgroups of drinkers (Satre et al., 2004).


Adults over 80

Those who are over 80 years old are considered the oldest of older adults. The number of individuals in this age group is increasing, as life expectancy increases (Sinyor et al., 2016). They are considered at higher risk for depression, other mental health issues, and suicide (Sinyor et al., 2016). Many of these individuals are residing within long-term care settings such as nursing homes, where estimates of substance use disorders, including alcohol, impact 50% of the residents (Sorrell, 2017). Careful consideration of medications for these individuals is necessary, yet the research is lacking for application to this age range (Hassell et al., 2017). For example, although daily doses of aspirin have been recommended by many physicians as a preventive measure for heart disease, there is limited data on the use of aspirin in people older than 80 (Xiong & Kenedi, 2010). The attending physician must determine whether the risks of aspirin use in a patient over the age of 80 outweigh the potential benefit and make the appropriate recommendations. Certainly, this is true of any prescription or over-the-counter

medication for any individual, but with those over 80, extra precautions are needed, and allowing for the individual to be involved in the decision making is essential when possible (Stone, Intwala, & Katz, 2014). As the population continues to age, further research on medications, medication interactions, treatment, and training of professionals interacting with this age group will continue to be essential to best help those who are over 80.

Chapter Summary

Although they are often overlooked as having or potentially developing SUDs, it is imperative that professionals consider the risk for SUDs in older adults, as well as risks due to multiple medications and health issues they may be encountering. This chapter covered the scope of SUDs in older adults, as well as the consequences of SUDs for this group. Additionally, the challenges in identifying SUDs within this group of individuals was discussed, as well as considerations for the subgroup of the oldest older adults.



CHAPTER 23

Substance Use Disorders and the Family

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 23.1** Understand the ways in which SUDs impact the family
- 23.2** Consider the multiple influences that impact how SUDs are managed in families
- 23.3** Describe interventions that may be helpful with families impacted by SUDs
- 23.4** Review the history and criticisms of the Adult Children of Alcoholics movement

Outside of residence in a concentration camp, there are very few sustained human experiences that make one the recipient of as much sadism as does being the close family member of an alcoholic.

—Vaillant (1995, p. 22)

Introduction

A conservative estimate suggests that one in every five adults has a close relative who has a substance use disorder (SUD) and that four or five people are hurt by the behavior of each person with SUD (Capretto, 2007). The most common source of such pain is through parental alcohol use disorders (AUDs). In spite of this fact, there has been little research into the issue of how parental AUDs might alter familial dynamics or the interaction pattern within the family (Green, 2006). Further, in spite of the awareness of the widespread problem of adolescent SUDs,¹ there has been little research to date into how the SUD of a child influences family dynamics. There are many theories and personal beliefs but little hard data on which to view the impact of the SUDs on the family unit, or to guide intervention efforts. In this chapter, the theories about, reactions to, and supporting evidence of the impact of a substance use disorder in the family will be explored.

¹Discussed in Chapter 20.

Scope of the Problem

Some researchers estimate that approximately 9.6 million children in the United States currently are living in a home where at least one parent has an active SUD (Capretto, 2007), whereas others estimate this to be more than one in ten for children under age 18 (Lander, Howsare, & Byrne, 2013). This figure underestimates the full scope of the problem because, as discussed elsewhere in this text, individuals tend to alternate between periods of more or less alcohol or drug misuse; perhaps twice this number of children are living in a home where one or both parents have misused one or more chemicals in the past year (Capretto, 2007). By the time they reach adulthood, more than one-half of the adults in the United States will have lived in a family where one member has, or at least had, an alcohol use disorder (AUD)² (Grant et al., 2006).

Addiction and the Family Unit

There are a number of variables that influence the impact of SUDs on the family. Some of these variables include (a) the number of people in the family who are misusing chemicals, (b) the role of the person within the family unit, (c) the presence of compensatory mechanisms within the family unit (grandparents, aunts or uncles, siblings) and role models outside of the family, and (d) the level of acceptance of the individual's substance use by family members, to name just a few.

Relationships are defined by the energy and information flow patterns between the members of the dyad (Siegel, 2013). Open lines of energy and information flow are characteristics of healthy relationships, while closed lines of energy and information flow patterns reflect the opposite (Siegel, 2013). Some of the information flow within the family takes place not by formal instruction but by observation or blind obedience to parental edicts even if they are dysfunctional (Hart, 2013). In this manner, "the *intergenerational transfer* of patterns of communication are reinforced by the repeated experiences of dysfunctional energy and information flow exchange patterns" (Siegel, 2013, pp. 2–3). This might explain why 11% of married men and 5% of married women raised in a family with a member who struggles with an SUD will themselves meet the criteria for an alcohol use disorder at some point in their lives (Lau-Barraco, Braitman, Leonard, & Padilla, 2012). The fact that most families with a parent with an SUD also suffer

from a wide variety of other issues such as mental health problems, underemployment, and financial issues (all conditions that would limit the flow of information and energy within the family), which contribute to the observation that even a moderately disturbed home environment can induce epigenetic changes in the affected family members that might last for years and be passed from one generation to the next (McCarrey, 2015; van der Kolk, 2014).

Alcohol is the substance most commonly misused in this society, and it will be used as the prototypical SUD for this chapter. The relationship between the alcohol use disorders and marriage is a complex one. The team of Kendler, Lonn, Salvatore, Sundquist, and Sundquist (2016) found that marriage appeared to serve a protective effect against the development of an AUD, with married participants in their study being 60–70% less likely to develop such a condition. The authors cautioned that the manner in which their study was carried out did not allow for clear cause-and-effect relationships to be identified.³ In marriages where one partner has developed an AUD, clinicians are often asked by the spouse of the person who misuses substances how his or her partner developed an SUD when he or she seemed so normal during courtship. The answer is complex: During the courtship phase and the first year of marriage, alcohol (and by extension other drug) misusers commonly reduce their level of alcohol intake (Leonard & Mudar, 2003). There is also a shift in relationship patterns following marriage: The individual typically spends less time in non-marriage-centered social activities (or spends more time with their partners, depending on how you look at it) (Leonard & Mudar, 2003). Another possibility is that the person with an AUD selects a partner whose alcohol use pattern is very similar to his or her own (Grant et al., 2007). A fourth possibility is that the substance misuser selected a partner who will tolerate the chemical use. Fifth, there is the possibility that the person misusing substances did not become enticed by the chemical(s) until after encountering the pharmacological reward potential of that compound after the marriage ceremony. Finally, one partner might engage in "secondary denial," either in courtship or in the first years of marriage, avoiding conscious awareness of their partner's AUD (Benton, 2009, p. 109).

The Family System's Perspective

This theory holds that people tend to select partners who have achieved similar levels of "differentiation of self"

²The differences between these two estimates reflect, in part, how "family" is defined in each study. For example, would a second cousin with an alcohol use disorder who lived 1,000 miles away be defined as a family member in both studies, or only in one study?

³These findings appear counterintuitive and may reflect cultural differences between Sweden, where the authors carried out their study, and the United States. It is also possible that the researchers' results reflect intergenerational effects, since earlier research studies were carried out on generations that came of age in the 1950–1980 era.

(Bowen, 1985, p. 263). From this perspective, each partner has achieved a similar level of emotional growth or maturity, although each partner follows a separate path in their quest to accomplish this developmental task. There is no single path to growth: Some paths are more adaptive and healthy, and others are just the reverse, but the process of growth continues, or at least tries to continue throughout the stages of ego growth. For the child, the main developmental goal calls for the individual to separate emotionally from one's parents (**individuation** or **differentiation**), allowing the emotional attachments to the parents that evolved in childhood to change as the child matures (Cozolino, 2017; Ross & Fuentres, 2010). In the healthy family, the child gradually learns to identify both the needs of the self and those of others, while growing in her or his ability to self-regulate emotions and be available to nurture others (Cozolino, 2017).

During the first year of life, the infant is almost totally dependent on the parents. Later, the child's ego growth is demonstrated through behaviors such as independent play, spending time with friends, etc. In the healthy family, the parents recognize this and gradually withdraw control as the child becomes more capable of independent living and self-nurturance.⁴ However, in the dysfunctional home parental conflict interferes with this process. In normal families, the child's attachment bonds to the mother enhance the growth of conflict resolution skills and relationship competence, while the attachment bonds to the father enhance the growth of social skills, relational competence, and emotional adjustment (Ross & Fuentres, 2010). These attachment bonds are not interchangeable but are complementary.

Frequent parental conflict, such as that between a spouse with an SUD and a spouse who does not misuse substances, weakens the child's attachment process to either parent. In the dysfunctional home, parental conflict is quelled through the establishment of a pseudo-stability in which certain issues are avoided and certain behaviors are not discussed. The child's emotional attachment to one parent is often discouraged or punished by the other. Emotional "power blocks" develop as conflict erupts within the family. The partner that does not have an SUD, or children, might assume roles that the partner misusing substances either does not feel capable of filling, or that he or she willingly relinquishes to focus attention on continued substance use. As a result of this change in familial roles, marital partners or family members may find themselves holding powerful positions within the family normally occupied by the person misusing substances,

which they are unwilling to give up should the parent misusing substances learn to face life without the chemical(s). The transition back to allowing the person misusing substances to fulfill his or her role in the family is often difficult.

Further, the child's growing emotional independence threatens the family's pseudo-stability. In the normal family, age-appropriate **differentiation** is encouraged. Maté (2010) offered what is perhaps the best definition of differentiation: "the ability to be in emotional contact with others yet still autonomous in one's emotional functioning" (p. 237). However, individual autonomy in emotional functioning might threaten the family's pseudo-stability. In response to the perceived threat of differentiation and separation by the child, the parents might respond with increased efforts to force the child to identify with the rules of the family system and not seek a separate identity (Cozolino, 2017). The pseudo-stability must be protected at all costs! The primary means by which parents attempt to maintain control and discourage emotional independence are *anxiety, guilt, shame, and threats of abandonment* (Cozolino, 2017). Abandonment can be on both a conscious and an unconscious level. Consider, for example, the hypothetical case in which a father selectively spends more time with a compliant son than with a more vocal, defiant child, even if that defiance is age-appropriate and the child's behavior is reasonable. Guilt is another powerful weapon employed in this process of enforcing parental control in the name of pseudo-stability. For example, at the funeral of a hypothetical 18-year-old boy who died in a motor vehicle accident the mother might turn to his older sister who was going to college far from home and say, "This would never have happened if you were here to keep an eye on him." The sister's decision to attend college threatens the familial pseudo-stability in this example because the parents have no control over what their daughter learns while she is away at school. Yet another example of manipulative guilt is the "silent treatment," where one or both parents simply stop talking to the child or adolescent until he or she apologizes, agrees with the parent's decision, etc.

Shame is a powerful emotion that is used in dysfunctional families to punish the child for any deviation from parental expectations. The victim of the shame attack becomes motivated to escape, often by (a) compliance with parental expectations or (b) detachment from their own emotions to survive. In this manner, the child learns to follow the family's rules to escape from the layers of shame and guilt that they are taught are rightfully theirs if they should deviate from the familial rules. Mixed messages are another way many parents use to control their child. The child or adolescent is locked into a choice between two mutually exclusive choices. Then the parents confront the child or adolescent for making the "wrong" decision, a process

⁴There is a difference between the gradual transition between parental control to self-control as the child matures and a lack of parental supervision.

that usually involves guilt (“If you had listened to me . . .”). Another way some children use to cope with a dysfunctional home environment is simply to run away.

Parental Rules

In many dysfunctional families, three “rules” evolve to maintain the pseudo-stability within the family: (1) don’t talk about the problem, (2) don’t have your own thoughts or feelings about the problem, and (3) don’t trust anybody (Capretto, 2007). Within the framework of these rules, the child is forced to rely only on the parents for guidance and support, especially during the child’s early, most formative years. If the child does not recognize that his or her parents are dysfunctional in early childhood, the child will internalize the parent’s opinions and beliefs, transmitting the parents’ problems to the next generation when he or she in turn becomes a parent.

If the child should fail to receive positive feedback and parental support for the quest for emotional independence, the growing child might come to view him- or herself as being weak, incompetent, and incapable of standing alone. The family, especially the parents, might reinforce this assessment of the self, discouraging further moves toward autonomy. The child begins to believe “I am not worthy . . . I am damaged . . . unable to stand on my own” (Juliana & Goodman, 2005; Sheff, Warren, Ketcham, & Eban, 2007). It is upon this shattered self-image that the child or adolescent will seek to build his or her adult identity. Such beliefs do not encourage the child to learn to nurture the “self,” which is one reason why the child will seek out external sources of feedback—all too often from the very dysfunctional people who raised the child.

Marriage with a Partner with an SUD

There are three common forces found in families where there is a substance use disorder: (1) the desire for stability, (2) the threat to the family stability, and (3) how the marital partners cope with issues (1) and (2). To complicate matters, the individual with the SUD does not have the same priorities as the partner: His or her priorities revolve around the continued use of the chemical(s) first, not the marital or familial unit. The SUD becomes a “silent partner,” first of the marriage and then of the entire family. Those who threaten to break the “no talk/no trust” rules identified above face possible emotional expulsion from the family (Dayton, 2005). This familial relationship style is then passed from one generation to the next. Children are taught not to trust their own perception(s) but to turn to others for guidance and support, even if these individuals are dysfunctional and do not have the child’s best interests at heart.

Marital Intimacy

In marriages where there is a wide discrepancy in the alcohol use pattern of the partners, there are usually lower levels of intimacy than in marriages where the alcohol use pattern of the partners is more similar. There are two possible explanations for this pattern: First, this might be a side effect of the individual’s alcohol use disorder, since it is known that alcohol can reduce the individual’s perceived need for emotional or sexual intimacy. Heavy alcohol use might induce sexual dysfunctions in both men and women. A second possibility, however, is that those individuals who are drawn to heavy alcohol use have fewer intimacy skills to begin with, possibly as a result of severe emotional abuse while growing up (van der Kolk, 2014).

Financial Stability

The addiction of one parent to alcohol places a financial burden on the entire family (Salize, Jackie, Kief, Franz, & Mann, 2012). The authors found that the direct costs for alcohol and related items consumed up to 20% of the budget of the typical family with a member with an AUD, a cost that fell to just 4% of the family budget if the family member with an AUD were to go to treatment. This is a contributing factor to the food insecurity problem briefly discussed in Chapter 20. The financial burden is just one factor that can contribute to a state of chronic stress for the child, in theory causing higher levels of illness on the child’s part (van der Kolk, 2014; Wyman et al., 2007). It is not yet known whether familial stress induces epigenetic changes in the child’s genetic heritage; however, the potential for such changes does apparently exist (Surani, 2016).

Although viewed universally as a negative influence on the marital unit, on rare occasions the SUDs serve as a *stabilizing influence* in some long-term relationships. It is thus imperative that the assessor determine the role the substance use disorder plays when conducting a substance use evaluation (discussed in Chapter 28). If the individual’s substance use is a stabilizing influence in a long-term relationship, then taking this coping mechanism away from the individual without replacing it with another, more effective one dooms the individual to relapsing should he or she attempt to quit misusing chemicals.

As control issues surface in the marital unit, family members begin to work at cross purposes, each side trying to change the other. **Conditional love** becomes a weapon used by one or both sides to impose their will on the other. This conditional love threatens the other with a withdrawal of affection and support unless he or she adheres to the demands of the other. It also becomes a justification for continued substance use by the partner with the SUD, since he/she is

obviously misunderstood, mistreated, and not loved (at least in his or her eyes) by the partner who is using conditional love as a weapon.

It is important to remember that at all times the family will seek to establish at least a pretense of stability if not actual stability. This is true in spite of boundary violations, psychosocial problems, and continued substance misuse by important members of the family unit. One way that this pseudo-stability is protected is that the unhealthy behaviors of the dysfunctional partner are exempted from scrutiny. “We came here for *marital* counseling,” the couple screams, “not to discuss [insert name here]’s drinking problems!!!” The parent who brings their child in for treatment of depression might stomp out of the session in anger if a parent’s drinking behavior is revealed, and the parent might refuse to pay for services rendered since this was not why they brought the child in to see a mental health professional!

Since the substance use disorder in the family is exempt from discussion, the family is forced to choose between (a) breaking the injunction against confronting the problem directly and (b) finding an alternative, less threatening way to adjust. Silence (often expressed as avoidance, rationalization, or denial) may be viewed as a safer alternative to confronting the problem. This is the foundation of the “no talk rule,” which holds that no matter how obvious or obnoxious the individual’s behavior might be, *nobody* will talk about it. This reduces the level of conflict within the family unit, and as such can be viewed as a short-term form of control over the issue. Another weapon often used in the quest for control by the non-abusing spouse is *emotional withdrawal*. Hurcom, Copello, and Orford (2000) discovered that almost 50% of spouses whose partners had a substance use disorder admitted to using this tactic at least on occasion. While the goal is that this will help the partner with the SUD reduce or stop the substance misuse, more often than not it has the opposite effect, since “a bottle,” as is often repeated at Alcoholics Anonymous meetings, “will never reject you.”

All of the conflicts discussed thus far often take place during a time when the child’s neural networks are still in a stage of growth and development (Sheff et al., 2007; Teicher, 2002). Studies continue to investigate the impact of constant stress on epigenetic changes to the individual’s genome, which may have lifelong consequences for the child (Houtepen et al., 2016). Parental conflict about a partner’s SUD occurs when the child is developing “core beliefs about security and safety” (Sheff et al., 2007, p. 7). The inability to trust their parents because of *their* ongoing conflict might encourage the children to develop a pathological self-sufficiency. The child assumes a caretaker role, staying awake while the parent is out drinking, checking on the safety of sleeping siblings, cooking meals for their siblings, and developing elaborate coping plans in case

of emergencies because the parent is emotionally if not physically unavailable. These are all responsibilities of the parent in a healthy home, but in the unhealthy home the adolescent might be forced to spend so much time and energy meeting basic survival needs that he or she is unlikely to have time to establish a strong self-concept or attend to other developmental issues of adolescence (Juliana & Goodman, 2005; Sheff et al., 2007). Extremes of abuse and neglect fostered by parental substance misuse, preoccupation with parental substance use, parental arguments about further substance use or possible divorce might also predispose the child to depression, anxiety states, suicidal thoughts or attempts at self-harm, impulse control disorders, and his or her own substance use problem later in life⁵ (Anda et al., 2000; Dube et al., 2001; Ross & Fuertes, 2010; Teicher, 2002). Unfortunately, children raised in such unhealthy environments frequently give off an aura of being mature, serious, and well-organized, behaviors that unfortunately mask the true nature of their internal distress, and are seen by others as signs of emotional maturity (Dayton, 2005; Ruben, 2001).

The home environment in which one parent has a substance use disorder is often marked by intrafamilial conflict. This, it has been suggested, contributes to children who seem to be “addicted” to excitement as adolescents (Ruben, 2001). According to this theory, the constant exposure to stress in the home leaves the child with the impression that anything less than the level of conflict experienced at home is abnormal, and so they engage in dysfunctional behaviors (for example, fire-setting), and later in life seek out partners who are likely to provide the desired level of excitement and allow them to feel “normal.” This then contributes to the tendency for the child to become involved in a dysfunctional relationship when they do achieve adulthood, as noted earlier.

Surprisingly, growing up in a home where there is a parent misusing substances does not *automatically* result in problems for the growing child. There are a number of factors that influence the impact of parental SUDs on the child’s emotional growth, including (a) the gender of the parent misusing substances, (b) the duration of time the parent misused chemicals, and (c) the availability of parental substitutes. The effects of a parent’s substance use disorder that was active for “only” 3 years will be different from those seen when a parent has been physically dependent on a chemical for the child’s entire life, for example. An uncle, neighbor, teacher, older sibling, or even a media star may offer the child a surrogate parent whose behavior might model more appropriate behaviors than does the parent misusing substances.

⁵ After all, who is going to help the child learn to control internal impulses, or develop healthy attitudes about substance use in a family such as this?

In order to adjust to a home where there is a parent misusing substances, adolescent children and the spouse sometimes spontaneously learn to *detach* from the unhealthy parent. Many therapeutic interventions seek to guide the family members to this point, which is paradoxically a reflection of *unconditional love* by family members. Through detachment, the child or spouse learns that “your behavior is *not* a reflection on me” and that “I love you enough to let you be independent, even if this means that you choose a path of destruction.” As part of this process, the individual learns to establish and maintain interpersonal boundaries (Black, 2003). This growth process can take many years, but in the end it blocks the unnatural enmeshment that had existed between family members, and makes the family member responsible for his or her behavior(s).

The Cost of Adolescent SUDs

Up to now, the discussion has focused on parental SUDs. However, the family member misusing substances might also be a child or adolescent. Surprisingly, there has been little research into how adolescent SUDs impact familial life. Families with an adolescent misusing substances do evidence (a) a lack of trust in the adolescent on the part of all family members; (b) a history of threats, abuse, and violence; (c) siblings who often are angry with the adolescent misusing substances for disturbing the familial tranquility; (d) a tendency for family members to isolate the adolescent misusing substances; and (e) a tendency for parents to be blamed for the adolescent’s substance misuse. There has been virtually no research into how adolescent substance misuse might affect the mental health of their siblings.

Interventions

The family in which there is a person misusing substances is often left to find a way to adjust to the problem on their own. However, there are a number of potentially helpful therapeutic interventions. The most effective of these interventions is known as *coping skills training* (CST). CST does not attempt to identify why a certain family member has a substance use disorder, and might not even include that person in the training sessions. The focus of CST is on helping family members learn how to cope with the behaviors of the person struggling with substance misuse. For example, if the identified patient has routinely asked for “loans” that were used to pay for alcohol or drugs, the CST program might focus on helping family members learn refusal skills. If the identified client should have a history of violence, the focus of the CST sessions might be on helping

the spouse identify available resources and explore legal options to deal with this violence. While the focus of CST is not to force the person misusing substances into treatment, one common result of such training programs is that the alterations in the client’s support group prove to be an incentive for the individual misusing substances to enter a rehabilitation program. Further, CST helps family members make the transition from being victims of the SUD to actively taking protective steps to cope with the individual’s SUD. Some research has identified *forgiveness therapy* and *conflict resolution interventions* as therapeutically useful for those who have grown up in a home with an SUD present (Osterndorf, Enright, Holter, & Klatt, 2011). Additional research has identified the importance of aiming intervention efforts at recovery for the individual with the SUD as well as improvement of the parenting skills of both parents (Bountress & Chassin, 2015). Ultimately, awareness is key for professionals working in all helping professions, to be able to identify families where SUDs potentially exist, to intervene as soon as possible for the benefit of the entire family unit (Lander et al., 2013).

The Adult Children of Alcoholics (ACOA) Movement

In the latter part of the 20th century, a number of adults stepped forward claiming that they were suffering from emotional dysfunctions that they attributed to parental substance misuse. Since parental alcoholism is more prevalent than the misuse of other chemicals, these individuals started to call themselves “*adult children of alcoholics*” (ACOAs). While the therapeutic focus has shifted away from the ACOA model, health care professionals will still occasionally hear from patients who identify as an ACOA, and research continues to explore the ACOA.

Surprisingly, there has never been a single, accepted definition of the “adult child” of an alcoholic parent. Ruben (2001) suggested that the term “carries a double meaning: an adult who is trapped in the fears and reactions of a child, and the child who was forced to be an adult without going through the natural stages that result in a healthy adult” (p. 8).

Proponents of the ACOA model hold that the child raised in a home with parental alcoholism were emotionally scarred for life (Ruben, 2001). Because of the parental AUD, the child would (Ruben, 2001; Woititz, 1983) (1) have to guess at what normal behavior was in social situations, (2) have trouble forming intimate relationships, (3) have difficulty following a project through from start to finish, (4) tend to lie in situations where it was just as easy to tell

the truth, (5) not feel comfortable with the “self” but constantly seek affirmation from others, (6) have trouble relaxing and having fun, (7) judge themselves harshly, (8) handle conflict situations poorly, and try to avoid conflict if possible, and (9) be loyal to others, even if that loyalty is misplaced (such as when they are physically or sexually abused, or their partner has failed to respect their loyalty).

Another characteristic of the adult child might include a tendency to self-sabotage (Ruben, 2001), as well as to express internal distress through conduct disorder or substance use disorders in childhood or adolescence (Fals-Stewart, O’Farrell, & Birchler, 2003, 2004). There is a danger that they will not allow themselves to exceed their parents’ level of competence or achievement in life lest they seem disloyal to their parents (Ruben, 2001). It has also been suggested that the traditional view of ACOAs is too narrow, and that some adult children develop traits opposite to those expected of a child raised in a dysfunctional home. Thus, while some adult children do have trouble following through with activities, others become overly responsible, compulsive workaholics, and possibly overachievers (Ruben, 2001). It is important to note that many of the typical characteristics of ACOAs are overgeneralized, and can actually be considered harmful when making assumptions about individuals (Sher, 1997).

Hart and Fiissel (2003) explored the impact of growing up in a home where there was a parent with an AUD on the later adjustment on the individual. They found that the children of a parent with an AUD might be vulnerable to later physical illness as an adult, although the exact reason for the relationship was not clear. It was also suggested that being raised in a home where there was a parent with an AUD might predispose the individual to problems such as dysthymia, phobias, and anxiety disorders. Further research has found that there may be greater depressive symptomology experienced by ACOAs in young adulthood (Klostermann et al., 2011), whereas other research point toward greater mood swings in those who identify as ACOAs (Murphy & Kelley, 2015), as well as being potentially more likely to use alcohol earlier in life and more likely to use drugs (Braitman et al., 2009).

The Growth of ACOA Support Groups

ACOA support groups emerged in 1978, and grew more numerous at a phenomenal rate early on. At one point, it was estimated that 40% of adults in the United States were members of some kind of 12-step support group, of which the ACOA groups were the most numerous (Garry, 1995). This phenomenal growth was fueled by many different factors, such as the large number of adults who agreed that they had been hurt by parental alcohol use disorders and the desire of many people to find peace and resolution by

working through their feelings about their childhood experiences growing up with a parent with an AUD. The ACOA World Service Organization reports that there are around 1,500 meetings worldwide (Adult Children of Alcoholics, 2017).

Criticism of the ACOA Movement

There are number of criticisms of the ACOA movement. First, the theory that growing up in a home with a parent with an AUD *in itself* is sufficient to cause psychosocial problems for the children in that home when they reach adulthood has not been supported (Bijttebier, Goethals, & Ansoms, 2006), and much of the research thus far contains contradictory findings (Richards & Nelson, 2012). Further, the philosophical grounds on which the ACOA movement is based have been challenged because it is essentially:

an enterprise wherein people holding the thinnest of credentials diagnose in basically normal people symptoms of inflated or invented maladies, so that they may then implement remedies that have never been shown to work.

—Salerno (2005, p. 2).

Perhaps the ACOA movement is a natural reflection of the American culture at the end of the 20th century. In the last half of the 20th century, a “popular assumption that . . . without professional help most people are incapable of dealing with adversity” (Sommers & Satel, 2005, p. 6) emerged. This assumption is wrong, and has been called “*therapism*” (Sommers & Satel, 2005, p. 6). Although inherently flawed, this phenomenon spawned an entire industry that negated personal resilience or the idea that people might find a way to come to terms with adversity without professional intervention. The therapism industry maintained that to cope with trauma it was first necessary for the individual to express his/her feelings (with the assistance of a trained helper, who is often paid for this assistance), and then banish those feelings and memories from consciousness. Such techniques are supported by anecdotal evidence rather than scientific research.

By the 1990s, therapism had become big business. In retrospect, the only “research” conducted into the ACOA phenomenon was by publishing companies that wanted to identify and anticipate emerging market trends so that the next wave of “self-help” books might reach the largest number of people without helping them do more than spend their money on the latest craze in the self-help book market (Salerno, 2005). Such self-help books offered to help the reader relive traumatic events (possibly long forgotten)

under the guise of helping them, while informing them of their victimhood status and weakening the individual's coping abilities rather than assisting them in further growth (Salerno, 2005; Zur, 2006). Salerno supported this argument with the observation that self-help books have been on the market since the 1950s, if not longer, and there is little evidence that the rate of psychopathology in the United States has appreciably declined in that time.

It has even been suggested that the ACOA movement reflects the baby boomer generation's attempt to hold on to a portion of their childhood by repeatedly recalling or generating resentments from their own childhood while blaming the previous generation for perceived misdeeds. It is "fashionable to be a victim" (Zur, 2006, p. 49), and thus we can feel justified in failing to accomplish everything that we wanted when we were young adults while blaming our parents, or so it has been argued. Some individuals hold to this position so tenaciously that it is almost as if they were "addicted" to being in an ACOA or similar recovery group (Salerno, 2005).

The ACOA movement is based on what clinicians call the *damage model*. Proponents of this position hold that "all children are affected" by parental alcoholism, for example (Black, 1982, p. 27, 2003). Yet in spite of stridently vocal advocates, the damage model has not been supported in the clinical literature. Most people find ways to adjust to trauma. To examine whether the damage model did indeed exist, Bijttebier and colleagues (2006) examined data from a community sample of 10–14-year-old children from the Netherlands and Belgium who had a parent with an AUD, and found that they did not demonstrate higher levels of anxiety or depression when compared with a control group of children. The children did report lower levels of familial cohesion, which could contribute to the lower feelings of self-worth reported by the children, although it was not clear whether the lower levels of familial cohesion contributed to lower self-esteem, or just the reverse. Further, it was discovered by the authors that parental support by the nondrinking parent, along with peer group relationships, helped to mitigate the impact of the parental AUD.

Admittedly, some children are raised in terrible, abusive environments. However, the assumption that growing up in such an environment *automatically* results in lifelong psychological pain for everybody has not been supported (Bijttebier et al., 2006). Using the criteria advocated by proponents of the ACOA movement, virtually all children are raised in a dysfunctional home, since the "healthy" conflict-free family is a myth. There has been little research into what constitutes a "normal" family, or the limits of unhealthy behaviors⁶ that a family might tolerate and still provide a

healthy environment for the children. Yet it is on this weak foundation that proponents of the ACOA model claim that 96% of the population was raised in a "dysfunctional" home (Salerno, 2005). This 96% figure has not been supported, but some proponents of the ACOA model quote it as if it were an established fact.

People have been coping with what we would now call unhealthy environments for generations, and yet the species has survived. This may reflect individual resilience, which was originally overlooked by the ACOA movement, and social supports for the child being raised in a home where there is parental AUD. There is evidence that resilience involves a gene that is engaged in the synthesis of serotonin ("Resilience," 2006). *Resilience* does not mean that the individual is invulnerable to trauma, but that there is a natural development of the adaptive systems in childhood that may help the child resist the damaging effects of the environment (Blum, 1998; Masten, 2001). It is only when these protective mechanisms are overwhelmed by extreme events that the individual's normal growth is disrupted. However, resilient children are adept at finding ways to adjust to parental alcohol use disorders through the use of parental surrogates or peer group support, and a focus on future goals rather than on current familial disruptions (Hall, 2008).

It has also been suggested that the ACOA construct reflects an oversimplification of the developmental process (Zweig & Wolf, 1997). Simply naming a process does not imply that one understands it. An excellent example of this is cancer. Calling it "cancer" does not mean that its causes, controls, developmental process, or suppression are understood. Further, it has been suggested that the ACOA model often leaves the reconstructive process unfinished, failing to reach the deepest levels of the individual's psyche necessary for complete healing (Zweig & Wolf, 1997). Other detractors of the ACOA construct point to the emphasis of this model on what is called the "inner child," a phrase that has found its way into popular culture.

When ACOA proponents focus on the problems of their childhood rather than those of adulthood, their ability to cope is compromised. Even if this elusive creature existed, the inner child reflects a phase of life when the individual was emotionally, developmentally, cognitively, and socially immature. These conditions no longer exist for the individual, who has grown into adulthood, even if the ACOA insists on focusing on past trauma.

Finally, it has been suggested that the ACOA model is a white, middle-class invention, although there has been more recent research relating to African Americans (Hall, 2008; Steiker, 2013). Yet there are children who have been raised in homes where the parents misused compounds such as cocaine or narcotic analgesics, and the literature that explores

⁶If the truth be told, we all have some unhealthy behaviors.

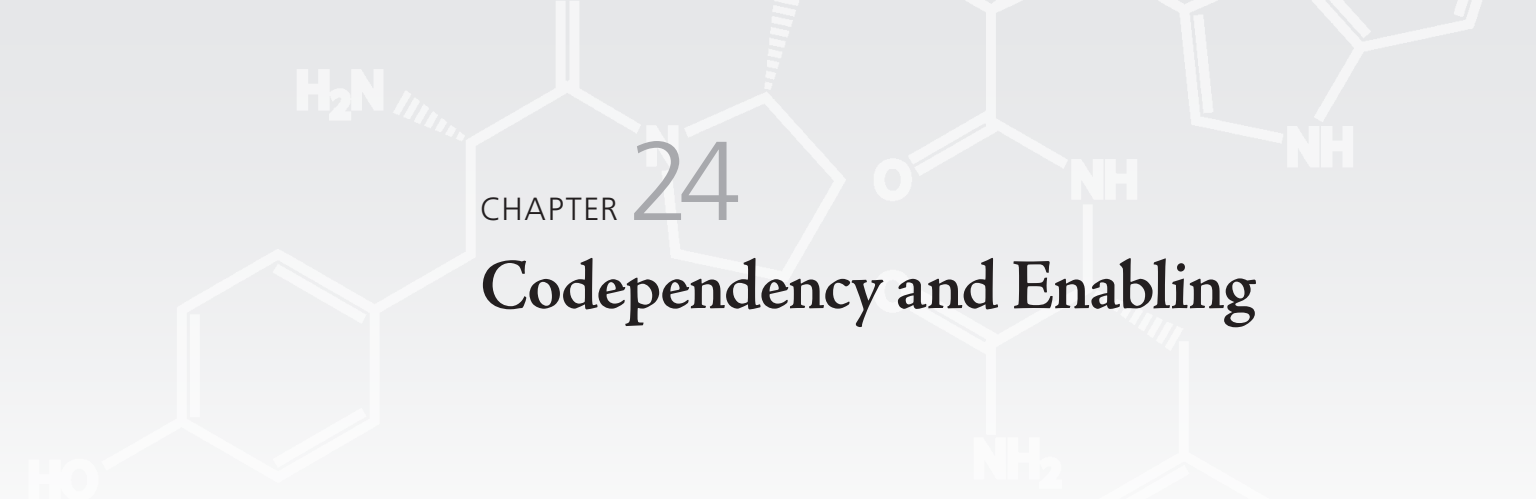
how being raised in such a home is quite limited. Given these challenges to the ACOA model, one must wonder whether the personality characteristics identified as having been caused by being raised in a home where there was a parent with an AUD reflect not psychopathology, but everyday problems in living. However, now, thanks to an overabundance of self-help books, we have a language through which we might blame earlier generations for the problems in life that we might encounter rather than taking steps to address them.

Chapter Summary

This chapter addressed the impact of parents struggling with substance use disorders on the family. While this topic is a popular one for general discussion, there are few clinical studies that explore the subject in detail. Further, it has been revealed that much of what is seen as true about the impact of parental alcoholism on the family is based on theory or personal beliefs, not research. On the surface, it would appear

that parental SUDs result in the child being “trained” to become dependent on external feedback, which then contributes to the development of codependency.

Arguably, proponents of the dysfunctional family model see only those individuals who have suffered as a result of parental SUDs. Those individuals who have found a way to adjust to their past are hardly likely to call attention to themselves as being dysfunctional because of their past. Parental alcoholism as the cause of psychopathology in family members has been met with skepticism, and the “adult child” concept has met with considerable criticism. Health care professionals point out that the damage model dismisses the possibility of individual resilience. This model automatically assumes that the experience of growing up in a home with a parent who has an SUD will result in trauma, a theory that has not been supported. Health care professionals also suggest that the paradigm of the adult children places too much emphasis on perceived past slights during childhood, at the expense of current life problems for the adult.



CHAPTER 24

Codependency and Enabling

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 24.1** Define and explain the concepts of codependency and enabling
- 24.2** Explain the connection between codependency and enabling and other terms typically used when codependency is discussed
- 24.3** Identify the connection typically drawn between codependency and mental health
- 24.4** Understand the typical reactions to the concept of codependency

Introduction

Health care professionals who specialize in the behavioral sciences are often faced with a bewildering array of behaviors that they must both categorize and try to understand. To help them in this task, mental health professionals use *constructs*: a form of professional shorthand that allows one professional to rapidly share complex information with another. A weather front is an excellent example of a construct. In reality, there are no lines that connect different weather cells, or firm boundaries between different bodies of air. By using the analogy of the battle lines of World War I, it was possible for meteorologists to develop a system that allowed them to portray complex data about changing weather patterns in a visual medium that other meteorologists could understand.

As mental health professionals began to explore the interpersonal dynamics within the families of those who misuse substances, they developed a number of new constructs to help them both understand and explain the impact of substance use disorders (SUDs) on both family members and others. Two of these constructs were *Codependency and enabling*, both of which were quite popular terms in the 1980s and early 1990s. They have become less popular in the 21st century, but because the terms were so popular, some mental health professionals will occasionally use one or both of these terms to summarize the complex dynamics within the families of those who misuse substances. Care must be taken in the use and interpretation of these terms when used by clients as well as by family members and other professionals. In this chapter, these constructs will be examined in more detail.

Enabling

To **enable** a person with an SUD is to *knowingly* behave in such a manner as to make it possible for that person to continue to misuse chemicals, or in a manner that protects the person misusing substances from having to suffer the natural consequences of her or his behavior. The paradigm

of “enabling” rests on the unproven assumption that within some families there is almost an unspoken conspiracy in which family members support the person’s continued substance use through these behaviors. Various theoretical reasons for these enabling behaviors have been suggested: Some family members feel threatened by a family member’s substance misuse and they enter a stage of *denial* to avoid recognizing the problem. This denial might be motivated by a desire to avoid perceived blame for the dysfunctional member’s behavior (Sadock, Sadock, & Ruiz, 2015). In other cases, family members come to enjoy the power and responsibility given up by the dysfunctional family member and are hesitant to give that power up when the individual misusing substances attempts to reassert his or her role in the family.

Some persons affected by the individual’s SUD are thought to become *overly protective*, confusing this protectiveness with an expression of love (Beattie, 2009; Ruben, 2001). For example, if the person with an SUD should be unable to go to work because of intoxication or postintoxication recovery, a parent or partner might call to report the person misusing substances as being “sick” and thus unable to go to work that day. In so doing, they hide the true nature of the family member’s problem and help him or her avoid the consequences of his or her behavior. Enabling behaviors might be motivated by a variety of other factors, including social pressure to be a “good” spouse, to avoid the loss of income should the dysfunctional family member’s behavior result in loss of employment, to fulfill the needs of the caregiver, or by pathological interdependency (Beattie, 2009; Sadock et al., 2015). These behaviors are found not only within the context of a family unit. An “enabler” might be a parent, sibling, coworker, neighbor, supervisor, friend, neighbor, or even a health care professional. Many health care professionals, for example, will not add a diagnosis of SUD to a patient’s file, for a variety of reasons. Some physicians rationalize this as being a way to protect the individual from the condemnation of society or from possible denial of insurance benefits at a future date. Others might wish to protect the family of the person with an SUD from the shame of having to acknowledge that such a problem exists in their home.

The essential point here is that the **enabler** is any person who acts to protect the person with an SUD from the full consequences of her or his behavior. Enabling behaviors are not limited to those who are in the family member’s immediate environment. The witness who refuses to testify against a criminal because he or she does not wish to become involved, because of the inconvenience, or out of fear of reprisal might be said to have enabled that person’s criminal behavior.

Codependency

The concept of *Codependency* emerged in the last quarter of the 20th century, and it remains both a popular construct used in “pop” psychology and one of the cornerstones of rehabilitation programs. In spite of the fervor with which some rehabilitation professionals preach that many of us are Codependent, it is important to keep in mind that this is a *construct*. Indeed, this is seen in the fact that there is no standard definition of Codependency, and various rehabilitation professionals argue over whether it should be spelled as one word (Codependency) or is possibly hyphenated (Co-dependency), although the former spelling appears to be slowly winning out (Jaffe & Anthony, 2005; Sadock et al., 2015). Another controversy is whether it should be spelled with a capital “C” (“Codependency”) or a lowercase “c” (codependency). As will be discussed later in this chapter, there has been strong disagreement among professionals about the validity of this construct (Blume, 2005).

Codependency Defined

For decades, family members have been quietly discussing how they have suffered, and often continue to suffer, from ongoing relationships with a person misusing a substance or substances. Gwinnell and Adamec (2006) defined Codependency as an “unhealthy relationship in which a person who is closely involved with an alcoholic or addicted person . . . [and] acts in such a way as to allow the addict to continue the addicted behavior” (p. 68). This relationship pattern usually is seen in a familial unit, although it might also exist between close friends, between an employer and an employee, or even between a police officer driving a person under the influence of chemicals home! Yes, in some communities, the police will simply escort the driver home, with the warning that the individual should not drive again until sober. This does place the police officer and the employer (the community for which the officer works) at risk for liability should the intoxicated individual not heed this warning.

Beattie (2009) observed that *caretaking* is at the heart of Codependency, with the person struggling with Codependency placing the needs of others above his or her own. This is often done with the goal of giving the person struggling with Codependency a purpose for living and a reason to fill the sense of emptiness that he or she feels within. This behavior also allows the individual struggling with Codependency to appear as if the person struggling with an SUD

¹ The uppercase C will be used throughout this text in the word “Codependency.”

desperately needs him or her. In such a scenario, the person struggling with Codependency will have little invested in having the person with an SUD recover, as this would leave him or her without a purpose in life. This is similar to how Blume (2005) defines Codependency “loosely as emotional dependence upon the person with a drug problem” (p. 168).

Various core components of the theoretical concept of Codependency have been advanced over the years, including (a) over-involvement of family members with a member with an SUD, (b) obsessive attempts on the part of the person with Codependency to control the behavior of the person with an SUD, (c) a tendency to base self-esteem on external sources of feedback, and (d) a tendency to make personal sacrifices in an attempt to “cure” (or at least limit) problem behavior of the person with an SUD. These behaviors are all externally focused, which is to say that the focus is only on the person with the SUD and not on the person with the Codependency.

The Relationship Between Enabling and Codependency

The reader will note that this chapter started with a discussion of enabling and not Codependency because these two constricts are deeply intertwined. To confuse matters, they both might be found in the same person, although this is not always the case. *Enabling* refers to specific behaviors, while *Codependency* refers to a relationship pattern. Giving money to a person who is homeless and has an assumed SUD might enable that person to buy more alcohol or drugs. The donor might suspect that the recipient will use the money for this purpose (enabled the recipient of the money) but does not need an ongoing relationship with that individual. A diagram of the relationship between the two might look something like the one shown in Figure 24-1.

The Dynamics of Codependency

In brief, the essential element of Codependency is the inability or unwillingness of the individuals involved to say “no”

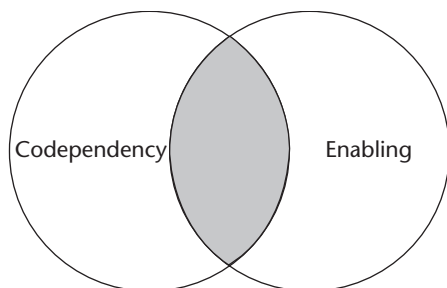


FIGURE 24-1 The Relationship between Codependency and Enabling Behaviors.

and set limits to the behaviors that they will tolerate (Sills, 2013). As a result of this failure at limit setting, the individuals' lives become unmanageable since they give control over their lives to another individual, the one struggling with an SUD (Beattie, 2009). Another danger of this process is that by giving control of his or her life over to the person with an SUD, he or she is in danger of becoming ensnared into assuming a caretaking relationship with the person with the SUD. Because of their discomfort or inability to set limits, the person struggling with Codependency might be afraid to leave the family member, or even be afraid of confronting him or her about the behavior(s). Further, because of a blurring of boundaries within the familial unit, the person struggling with Codependency begins to believe that the behavior of the family member with an SUD is somehow a reflection on him- or herself. This process of extreme involvement in the life of another person illustrates the boundary violations often seen in Codependency known as **enmeshment**.

Enmeshment, also called *fusion* in some schools of thought, is seen as based on the individual's unconscious fear of abandonment (Dayton, 2005). The self-esteem of the person with Codependency is threatened by the other person's behavior, especially the threat of abandonment. To avoid this risk, the person with Codependency often places personal aspirations and desires aside and devotes all his or her energy to the care-taking process (Beattie, 2009; Johnson, 2003). An extreme example of this might be seen when the person struggling with Codependency assumes responsibility for the other person's substance misuse, blaming him- or herself for the other person's use. Involved professionals and friends of the person with Codependency are used to hearing phrases such as “I made [insert name here] so upset that [he/she] started drinking again!” reflecting the belief that “It's all my fault.”

An extreme example of caretaking is the attempt to control the person with an SUD and his or her environment. For example, consider a hypothetical case in which a prison psychologist receives a telephone call from the elderly mother of an inmate. She asks that the psychologist “make sure that the man who shares my son's cell is [going to be] a good influence on my son,” because “there are many bad men in prison and I don't want him falling in with a bad crowd.” This request ignores the grim reality that her son was not in prison for singing off-key in choir practice, and in this example that he had a history of multiple prior convictions. The mother in this case might be said to be in serious denial about her son's behavior, as well as so involved in her son's life that she was still trying to control and “cure” him, in spite of the thick prison walls and the armed guards.

In this hypothetical example, the mother might become quite disturbed when it is gently suggested to her that she needs to *detach* from her son and his dysfunctional behavior.

Detachment is considered one of the cornerstones of recovery from Codependency (Beattie, 2013; Brown & Lewis, 1995). Through this process, the person struggling with Codependency learns to “let go” and stop attempting to control the other person’s life (Beattie, 2013). However, it is a difficult lesson to learn for many who have invested so much of their lives to the process of caretaking. Perhaps, in the example provided above, the mother’s intentions are good, but her efforts reflect an over-involvement with her son’s life.

Another core element to Codependency is *control* (Beattie, 2013). Through various adaptive behaviors, the person with Codependency is viewed as attempting to achieve a sense of control over his or her own inner turmoil, and over the dysfunctional person (Craig, 2004). Sometimes the person struggling with Codependency sets the goal of “fixing” the other person, so that he or she will no longer engage in inappropriate behaviors. Perhaps, they reason, the other person will then come to appreciate the Codependent’s efforts (Knauer, 2002; Ruben, 2001). However, this attempt at control often results in criticism of the person with Codependency by the person struggling with the SUD, who does not understand (or appreciate) the sacrifices made by the person with Codependency. A variation of this approach is seen when the person with Codependency adopts a self-pitying approach. Guilt becomes the weapon here (“If you really loved me, you would stop . . .”) (Johnson, 2003); however, this attempt at control becomes meaningless if the person with the SUD does not feel guilty. Other individuals adopt a rigid, controlling approach, seeking to stabilize the home through rules and repetition, to limit (if not eliminate) the dysfunctional behavior(s) by the other (Johnson, 2003).

The Rules of Codependency

Although persons with Codependency often report that they feel as if they were going crazy, an unbiased outside observer will carefully note that there are certain unspoken rules within the family unit. Beattie (1989) identified several of these rules:

1. It is not OK for me to have personal feelings.
2. It is not OK for me to have problems of my own.
3. It is not OK for me to have fun, or a life of my own.
4. I’m not lovable and should feel grateful for the affection I receive.
5. I’m never good enough.
6. If people act crazy, I am responsible.

These rules are actively transmitted within the family, setting the foundation for Codependency: “If you did what I told you, I wouldn’t have gone out drinking last night!” is an example of rule number 6. “College! Don’t even waste your time applying, you’ll never make it!” is an example of rules 2, 3, 4, and 5. Through the transmission of these rules, the person’s will

is broken and she or he becomes so emotionally intertwined with the person with an SUD that in extreme cases he or she becomes unable to identify his or her own feelings when asked.

There is an inherent power struggle between the family member with an SUD and the family member with Codependency: The person with Codependency wants to control the behavior of the person with the SUD to keep peace within the family and avoid conflict. The family member with an SUD wants to shape the family member with Codependency so that he or she will not challenge his or her inappropriate behavior(s). An all-too-common experience for helping professionals is for one partner to set up an appointment to ask that the helping professional “fix” the other person. Often, nobody has even asked the second person if he or she sees the behavior(s) in question as a problem or if he or she wants to be “fixed.” A hypothetical example might be the situation in which the husband is using cocaine at the time when he and his wife enter marital therapy. The husband demands that the therapist should “make her stop nagging me” without revealing his cocaine use. The wife also avoids mentioning her husband’s cocaine use (remember: appearances are everything), although it readily becomes apparent that her “nagging” reflects an attempt to control her husband’s behavior for an unknown reason(s). Sadly, to protect the disclosure of the husband’s cocaine use, this hypothetical couple might resort to dropping out of marital therapy.

Are Codependents Born or Made?

Some proponents of the concept of Codependency suggest that it is a *learned* relationship pattern, possibly the result of physical, sexual, or extreme emotional abuse during childhood (Knauer, 2002). For example, the child experiences a boundary violation with each episode of abuse. If the child is not rescued by a protector, he or she learns to tolerate those boundary violations that he or she is helpless to prevent. Through this process, the individual is taught that he or she is “less than” others, not worthy of ordinary levels of respect or independence (Knauer, 2002). The child also might wrongly assume responsibility for familial problems beyond his or her control, especially if he or she is blamed for these issues by significant others. For example, imagine a child being told, “Your father and I never argued before you came along.” Over time, the child learns to accept the dysfunction as the norm, and is socialized into accepting the role of a Codependent (Zelvin, 1997).

It is within this flawed, painfully dysfunctional environment that the young person with Codependency attempts to build a self-image. Communication between family members becomes limited to “safe” topics that will avoid giving the person misusing substances another reason to have a temper outburst, engage in substance use, etc. The children quickly learn that *nobody* mentions the inappropriate behavior by the person with an

SUD. “Don’t say anything about [insert the inappropriate behavior], or else [the person with an SUD] will become upset!” is a common message to the child in such unhealthy homes. In cases of physical, emotional, or sexual abuse, the child is taught not to discuss it with others in order to maintain an uneasy façade of family cohesion and peace. Frequently, the child learns to avoid facing intense negative feelings within themselves brought on by the abuse, and learn to live a rigid, compulsive lifestyle focused on meeting the needs of the other person (Craig, 2004).

Codependency and Self-Esteem

In an attempt to maintain peace, the person with Codependency learns that his or her emotional pain is subservient to maintaining that peace, a process known as *emotional constriction*. They are taught that they do not deserve to express their own emotional pain as it is unimportant compared with the goal of maintaining peace in the relationship. The constant erosion of interpersonal boundaries and of being *told* what the person with Codependency is (or should be) feeling eventually has a negative impact on his or her self-esteem, which might become so undermined that the person finally interprets protecting the *family secret* as the measure of their self-worth.

To protect the family secret, the young Codependent might watch as others engage in *denial* (“Your uncle is *not* an

alcoholic, and I never want to hear you mention his drinking again,” for example) and *minimization* (“Oh, it’s not so bad”). The family might not foster feelings of independence and competence within the family unit because these things would potentially shatter the wall of denial within which the family has surrounded the problem. This leaves family members, especially children, vulnerable to feelings of low self-esteem: They are not rewarded for positive accomplishments but for not asserting themselves and their caretaking of the person with an SUD. The expectations for caretaking are recognized as unhealthy by the person struggling with Codependency, and they often cannot envision another way of living. They often take pride in how much they have suffered, a behavior learned in childhood, and interpret their suffering at the hands of another as a form of moral victory or an affirmation of love. Because they are unable to envision any other way of living, these trials become almost a badge of honor, and a defense against the feelings of worthlessness felt within.

The Cycle of Codependency

Once the cycle of Codependency has started, it takes on a life of its own. A graphic representation of the cycle of Codependency might appear something like Figure 24-2. In the figure, there are two essential elements. First, the person

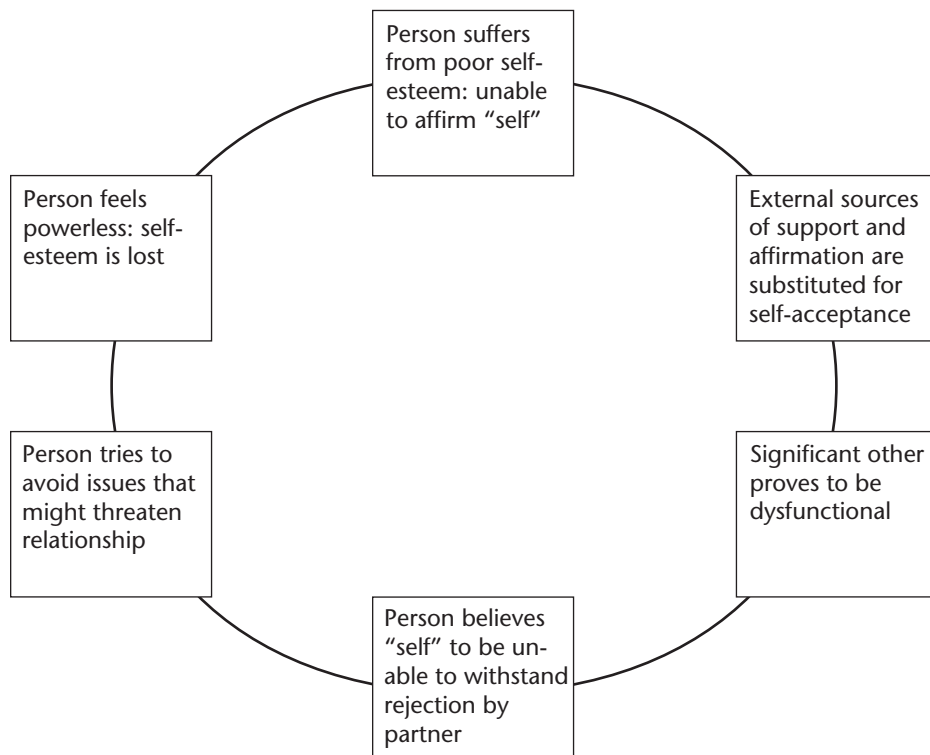


FIGURE 24-2 The Cycle of Codependency.

with Codependency must suffer from fragile or low self-esteem. If the person had adequate self-esteem, then she or he would be able to affirm “self” without external validation, and thus not be vulnerable to the other person’s threats to withdraw affection or support. The self-affirming person would draw away from the person with the SUD, thus blocking the unhealthy relationship from evolving in the first place. The second element is that the significant other struggling with an SUD consciously or unconsciously reminds the person struggling with Codependency of his or her original home environment.

A central tenet of psychoanalytic theory is that we create unresolved childhood conflictual relationships in later life in an attempt to find closure. A common experience for substance rehabilitation professionals is to find that the spouse struggling with Codependency has replaced the family member with an SUD from childhood with the same type of person as a marital partner. Freud called this the “repetition compulsion,” a construct that suggests that individuals continue to struggle with unresolved issues from childhood until they are resolved. To the believer in the Codependency model, this relationship pattern is interpreted as the person struggling with Codependency being “addicted” to a dysfunctional relationship.

Patterns of Codependency

In the last quarter of the 20th century, professionals who work with those with SUDs attempted to group common coping styles used by people struggling with Codependency. A number of such adjustment styles have been suggested, including those listed in Table 24-1.

The Codependency model maintains that family members of a person struggling with an SUD will adopt one or more of the coping mechanisms outlined above to deal with the stress that the person misusing substances places on the family unit. An example of the “co-conspirator” might best be seen in the hypothetical spouse of a person with a cocaine use disorder who wants marital counseling because the addicted partner will not limit her or his cocaine use to the \$100 a week, which was budgeted for the purpose. Other examples of this coping style might be seen in the partner who goes to the bar with the person with an alcohol use disorder to “try and show [him or her] how to drink in a responsible manner.” These efforts to change the family member’s behavior from within the family unit are usually doomed to failure.

A very good example of the messiah is the hypothetical father of a young adult with an opiate use disorder. In a therapy group for family members, the father tearfully discusses the litany of problems that the child has caused,

and how the parents repeatedly have to take out personal loans to pay off their child’s drug debts. Another group member suggests that the parents just force the wayward child to pay his/her bills and be responsible for themselves. The father thinks for a long moment and then says that if he did this their adult child “might leave us.” When several family group members suggest that this would not automatically be bad, the father quickly replies, “Oh, I couldn’t do that, [child’s name] is not ready to assume responsibility for [him- or herself] yet!” Thus, the parents continue to support their child’s OUD to avoid the short-term consequences of having the child become “angry” at them. Learning to say “no” to their child would allow the parents to place limits on which of their son or daughter’s unhealthy demands or behaviors they will tolerate. Limit-setting can be difficult at first, but with practice the individual setting the limits discovers a new degree of freedom for him or her “self.”

The Relationship Between Codependency and Mental Health

While this model of the interactional pattern within the home where there is a person misusing substances appears to make sense, there is a very real tendency for rehabilitation professionals to over-identify with the Codependency model. Even if the individual were to be Codependent, there are degrees of Codependency, just as there are degrees of heart failure, or obesity, or SUDs. Using a very liberal interpretation of the criteria virtually “anyone is codependent” (Beattie, quoted in Tavis, 1992, p. 194), and that Codependency “is an exaggeration of normal personality traits” (Cruse & Wegscheder-Cruse, 2012, p. 43), only a few “saints and hermits” (Tavis, 1992, p. 193) fail to demonstrate at least some of these behaviors on occasion. The Codependency model does not address the fact that many of the same behaviors outlined in Table 24-1 are also found in healthy family relationships. Thus, Codependency may actually be a reflection of the individual’s ability to adapt to life circumstances using a range of healthy adaptive techniques. The person struggling with Codependency reportedly tends to over-use just a limited number of the coping styles, and frequently bases his or her self-esteem on their success at carrying out their role as a Codependent (Cruse & Wegscheder-Cruse, 2012).²

² Rychtarik, McGillicuddy, and Barrick (2015) identified the initial model of a web-based support system for codependent persons to help support their self-esteem without encouraging them to engage in codependent behaviors.

TABLE 24-1 Common Coping Styles for Persons with Codependency

Coping Style	Goal of Coping Style	Coping Style	Goal of Coping Style
Apathetic partner	Might also be called “silent sufferer”—the partner simply stops caring (emotional shutdown often seen with this pattern of coping)	Family mascot/clown	Family member who tries to deflect attention from the substance-abusing family member to themselves, thus reducing risk of conflict in family
Approval seeker	Constantly seeks the approval/acceptance of the dysfunctional partner (for external validation)	Martyr	Self-righteous partner who receives support for being the “good” partner, substituting affirmation for lack of self-esteem
Caretaker	Devotes his/her life to taking care of the dysfunctional partner	Messiah	Fights against the dysfunctional behavior(s) in such a way that the individual is never forced to face consequences of their behavior (also called <i>chief enabler</i>)
Coconspirator	Consciously or unconsciously joins with the dysfunctional member to maintain pseudo-stability within the family (also called the “joiner”)	Protector	Seeks to maintain familial peace at any cost, even if it allows dysfunctional behaviors to continue
Controller	Engages in manipulative behaviors in an attempt to control every aspect of the life of the entire family, as they feel (often with some justification) that their own life is out of control	Persecutor	Blames everybody <i>but</i> the dysfunctional member for familial problems (may be called <i>get even</i> pattern of relationships)
		Separator	Over time spends less and less time at home, avoiding conflict that might otherwise exist in family unit

SOURCE: Based on Capretto (2007); Craig (2004); Ellis, McInerney, DiGiuseppe, and Yager (1988); Sills (2013); Johnson (2003).

As noted above, many of the behaviors used to define Codependency are exaggerations of normal behaviors. An example of this is the overlap between love and Codependency because of how love relationships are viewed within this society (Zelvin, 1997). Love is viewed as allowing for the blending of identities, and the weakening or loss of ego boundaries. This is perhaps a strength of love, but it also allows for Codependency to develop if it is taken to an extreme. Between the extremes of total independence (the “hermit” noted earlier) and total dependence on the other (the Codependent) is an *inter*-dependency, which is the hallmark of healthy relationships. Partners have the freedom to hold their own opinions, have their own hobbies, etc., which bring

variety to the healthy relationship without threatening it. Disagreements are resolved through discussion of the problem in the healthy relationship, with compromise and tolerance rather than threats or physical violence, as are so often seen in unhealthy relationships.

Reactions to the Concept of Codependency

It is important to remember that Codependency is a *construct*, which might be attributed to M. L. Lewis’s (1937) theory that the spouse of a person with an alcohol use

disorder (AUD) (usually the wife) had a disturbed personality and was trying to resolve her own inner conflicts through the marriage to a person with an AUD (Troise, 1993). Suddenly, the partner was classified as being dysfunctional, although in a different way than the spouse with the substance use disorder. From that point on, mental health professionals have struggled to determine whether Codependency is a legitimate form of psychopathology, a struggle that has not been helped by the fact that Codependency has been characterized as “an addiction, a personality disorder, a psychosocial condition, and an interpersonal style” (Hurcom, Copello, & Orford, 2000, p. 487).

As the last comment would suggest, Codependency is not a useful diagnostic category because it is too vague, and is not recognized by the American Psychiatric Association as a legitimate disorder in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013; Johnson, 2003). Not surprisingly, there is little evidence that Codependency even exists (Blume, 2005; Lilienfeld, Lunn, Ruscio, & Beyerstein, 2010). These doubts rest on the vague, ill-defined nature of Codependency, since virtually every person will have at least one of the defining characteristics. At what point, for example, does a mother’s natural protectiveness for her child become “overprotective”? How do you define “just protective enough” without going over that hypothetical line?

It is the opinion of many professionals that Codependency is a pseudo-problem more than a legitimate form of psychopathology, although some still hold strongly to the concept and continue to focus research in this area (such as Lampis, Cataudella, Busonera, & Skowron, 2017). Many health care professionals are uncomfortable with the Codependency model because it transforms a relationship style, even if it is an unhealthy one, into a medical problem (Hurcom et al., 2000).

Further, the application of the label “Codependent” to a marital partner *disempowers* the individual by expecting him or her to accept the label and seek help from the appropriate professional. The paradigm of Codependency is based on traditional 12-step programs for substance use disorders, which suggest that the “disease” of Codependency is progressive and can only be addressed by attending the appropriate self-help group (Randle, Estes, & Cone, 1999). This position rests on the assumption that “a knife wound to the chest will heal but an injury to the mind will never repair itself” (Sherwood, 2009, p. 286). The therapist, expecting certain characteristics in the patient, selectively attends only to those characteristics that conform to the preconceived construct of Codependency. Further, the counselor or group will “reward” individuals for using the terminology of Codependency, praising them for their courage in revealing things about their past.

Another challenge to the validity of the Codependency construct is the observation that up to 99% of adults in this country could be said to have been raised in a “dysfunctional” home,³ whereas in fact the majority of parents provide a “good enough” home environment. Admittedly, there is always room for improvement in parenting styles, but only a small minority of persons grow up in extremely unhealthy home environments. Further, in many cases even if a child is raised in an unhealthy environment, the possibility of resiliency within the child is all too often discounted in spite of evidence demonstrating that this is the norm and not the exception. Adversity often serves as a *stimulus* for personality growth and not automatically an experience that blocks adaptive growth (Sherwood, 2009). Children have been raised in incredibly unhealthy environments for thousands of generations, yet the species continues to thrive. It would not thrive if the majority of its members were hobbled with major psychological trauma from childhood. Admittedly, not every member of society is happy and content. However, there is little evidence suggesting that the individual *must* be happy and content to function in society. Indeed, some of society’s greatest leaps forward were initiated by those persons who were least content with the status quo.⁴ This observation is supported by the fact that the family is not (as is often suggested) an “incubator of [psychological] disease” (Kaminer, 1992, p. 12).

It has been suggested that self-help groups for Codependency misrepresent the promise of recovery while fostering dependence on the self-help group. In group meetings, the individual is expected to recover memories consistent with the group’s expectations, which is to say to continue to recall material and behave in a “Codependent” manner (Randle et al., 1999). Individuals who fail to follow the group’s expectations are said to be in “denial.” If the individual rejects the insights offered by various books on Codependency, she or he is also said to be in denial. Further, no matter how serious or slight the parental misbehavior, there is just one model for recovery they will consider: the Codependency model. All emotional trauma is viewed within this model as being equally destructive.

Critics of the model of Codependency point out that the construct seems to excuse the individual from responsibility for his or her behavior. Individuals just cannot help themselves because they are “Codependent.” Further, through the “disease” of Codependency, blame is shifted from the individual misusing substances to the significant other, who is automatically said to “enable” the partner’s dysfunctional

³ The concept of Codependency has been extended to include entire communities, states, and countries (Hurcom et al., 2000).

⁴ John Adams as a moving force behind the ratification of the Declaration of Independence leaps to mind, although there is a plethora of other examples throughout history.

behaviors. The behaviors of the person who is said to be Codependent are automatically deemed pathological, overlooking the fact that their behavior might be a healthy, role-specific response to the partner's substance use disorder (Hurcom et al., 2000).

Further, the Codependency model reflects the *family disease model*. This model suggests that “the solution is for each family member to recognize that he or she has a disease” (Fals-Stewart, O’Farrell, & Bircher, 2003, p. 148). The family member who has either a substance use disorder or the disease of Codependency is judged not on their own accomplishments, but on whether the family member with the SUD is able to abstain from chemicals. Family members are guilty by familial bonds with a using member misusing substances, and the “problem” becomes not that of substance misuse, or sexual misbehavior, or physical violence on the part of the dysfunctional person, but on *family* members who suffer from the disease of Codependency!

The Lewis (1937) model was advanced almost a century ago and was resurrected in the 1950s as a popular theory that the spouse was a co-addict (Sadock et al., 2015; Sher, 1991). This theory assumed that the spouse was as much in need of professional treatment as was the spouse misusing substances, because he or she (a) helped to cause the other's alcoholism, (b) continues to support it, and (c) thus obviously must be disturbed. These beliefs reflect the fact that throughout history the spouse of the alcoholic has “been blamed and pathologized for their partner's drinking” (Hurcom et al., 2000, p. 473). There has been little clinical evidence presented to support this theory or to suggest that the spouse of a person with an SUD has any consistent form of psychopathology, but this does not prevent the theory of co-addiction from being resurrected under the name of “Codependency.”

Another challenge to the Codependency concept was offered by Jaffe and Anthony (2005). The authors observed that the construct has been so watered down and misused that it has lost any possible hint of diagnostic specificity. This is seen in the definition of Codependency offered by Peck (1997), in which Codependency is viewed as “a relationship in which partners cater to—and thereby encourage—each other's weaknesses” (p. 180). This definition could be applied to virtually every relationship, since we all make provisions for the other person's quirks and idiosyncratic behaviors on occasion!

Many critics of the Codependency construct point out that it rests on little more than “new age” rhetoric. For example, the husband and wife team of Cruse and

Wegscheider-Cruse speak “knowingly” about how Codependency results from the

interactions between one's own manufactured “brain chemicals” (having to do with our reinforcement center) and one's behavior that stimulates the brain to establish compulsive and addictive behavior processes.

Cruse and Wegscheider-Cruse (2012, p. 22)

The authors go on to conclude that Codependency is a brain disease, on the assumption that:

we have a brain that gives us an excessive rush . . .
[and] we get into self-defeating behaviors that keep the rush coming (codependency).

Cruse and Wegscheider-Cruse (2012, p. 22)

Admittedly, the human brain evolved in such a way as to help us cope in a social environment (Gazzaniga, 2008). Further, the author suggested, interpersonal relationships affect the neurochemical balance within each individual's brain. *Any* life experience changes the brain's neurochemistry. However, there is no evidence that a relationship can cause an “excessive rush.”⁵ Nor has science found evidence that we get into “self-defeating behaviors that keep the rush coming.” This is not to dismiss the fact that there are many people who have suffered terrible psychological, and on occasion physical, injury from their involvement with a partner struggling with an SUD. To automatically classify them as Codependent without an investigation into the dynamics of the relationship is unfair. Further, the person labeled as Codependent is expected to come to terms with his or her pain, and achieve healing without blaming the addicted partner for virtually anything that he or she has done. In other words,

according to adherents of [the theory of Codependency], families of alcoholics can not . . . hold them [the addicted person] responsible for the abuse. Somehow the victim must get well by dint of pure self-analysis, meditation and prayer, without reference to the social, economic, legal and psychological forces that create[d] [the] dysfunctional families.

“Codependency” (1990, p. 7)

Chapter Summary

Every 20–30 years a theory is advanced suggesting that the spouses or family members of a person with a substance use disorder support that person's SUD through their own behavior. This was first suggested by Lewis (1937), and the theory was resurrected in the 1950s as a popular theory that

⁵ Which raises the question: What would be a sufficient “rush”? If something exists in excess, does this not imply that it also exists in a form where there is a sufficient supply, without being present in excess?

the spouse was a co-addict who was as dysfunctional as the individual misusing substances and who required professional assistance for this reason (Sadock et al., 2015; Sher, 1991). This theory was eventually dismissed. Then in the 1970s, the constructs of **enabling** and *Codependency* were introduced to help health care professionals view the individual with an SUD and his or her support system in a different light. The construct of enabling was introduced to explain how others might behave in a manner that supported the continued dysfunctional behavior of a person with a behavioral disorder. Through Codependency, family members, friends, employers, and others might be said to enter into a relationship that supported the continued misuse of alcohol or drugs by the identified patient. Proponents seized upon these constructs as proof that the disease of alcoholism (and, by extension, the other drugs of misuse) included not

just the person with an SUD, but others who also needed “treatment.” Self-help groups also evolved to meet the perceived need for rehabilitation by those who “suffered” from Codependency.

After the usual spell of initial enthusiasm, support for these constructs has faded. Indeed, in the first part of the 21st century, a battle has raged over whether these are real entities, just constructs that characterize certain behaviors, or pseudo-issues that cloud the problem of substance use rehabilitation. While there are certainly a large number of people who hold tight to the construct of Codependency, the negative message that one is responsible for another’s addictive behaviors has not aligned with the research or interventions for working with families and individuals impacted by SUDs (Calderwood & Rajesparam, 2014).



CHAPTER 25

The Client with Co-Occurring Disorders

Substance Use Disorders and Mental Illness

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 25.1** Understand and explain what constitutes co-occurring disorders of SUDs and other mental illnesses
 - 25.2** Identify the causal considerations for co-occurring disorders
 - 25.3** Consider the diagnostic challenges of determining accurate diagnoses when co-occurring disorders are present
 - 25.4** Understand the scope of the problem of co-occurring disorders
 - 25.5** Consider the relationship between drug of choice and psychiatric diagnosis
 - 25.6** Review the struggles that may be encountered in working with clients with co-occurring disorders
 - 25.7** Identify current treatment approaches to working with those with co-occurring disorders
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Introduction

Two generations ago, many psychiatric textbooks suggested that substance use disorders (SUDs) in patients with mental illness were rare. This claim, based on clinical lore and a lack of research data, was found to be wrong. When epidemiological studies on the SUDs among those with mental illness were conducted, health care professionals were surprised to discover that not only do the two conditions often exist in the same individual, but that the majority of psychiatric patients have a co-occurring SUD (Buckley, 2006; Minkoff, 2008; Seppala, 2004). This knowledge was only the first step, as health care professionals still struggle to understand the complex relationship between SUDs and mental illness. Their confusion is perhaps best epitomized by the fact that clinicians have yet to even agree on whether to call these individuals client with **dual diagnosis** or **co-occurring disorder**, *mentally ill substance users*, or *mentally ill/chemically dependent* (MI/CD) patients. For the purposes of this text, the term co-occurring disorders will be used. It is recognized that each term is limited in scope, but we have to begin somewhere, do we not?

Although health care professionals now accept that individuals with co-occurring disorders are the norm rather than the exception, they still tend to view these patients as a single diagnostic category (e.g., “mentally ill substance abusers”) as opposed to a heterogeneous population with multiple pathways both to substance use disorders and to expressions of their mental illness (Hesselbrock & Hesselbrock, 2007). Thus, clinicians lack knowledge of such factors as those that initiate or maintain an SUD in those persons who have a mental illness (Drake, Mueser, Brunette, & McHugo, 2004; Petrakis, Gonzalez, Rosenheck, & Krystal, 2002). Research into effective treatment methods that might be most effective when working with the person with co-occurring disorders is in its infancy, and the research into how the effects of the drugs of misuse might help to suppress (or exacerbate) psychiatric symptoms is lacking. Substance use can simulate the symptoms of virtually all forms of mental illness, making a differential diagnosis difficult. In this chapter, the unfolding issue of how to identify and treat individuals with co-occurring disorders will briefly be reviewed.¹

Definitions

The previously used term, dual diagnosis patients, referred to those who suffer from a concurrent form of mental illness and a substance use disorder. Since this term may cause the incorrect assumption that there are only two, one mental illness and one SUD, the term **co-occurring disorders** is now preferred, since an individual may be struggling with one or more SUD along with one or more mental health diagnosis (Ekleberry, 2014; Smith, Drake, et al., 2010). Coexisting disorders are not difficult to understand. Patients often have more than one medical disorder: A patient might suffer from hypertension and obesity, conditions that may be interrelated and that may interact (if you lose weight, your blood pressure will probably drop in this hypothetical example). When discussing clients with co-occurring disorders, it is important to keep in mind that the SUD did not *cause* the mental health disorder, although it might be intertwined with it. This is an important point, because for decades it was believed that if you addressed the psychiatric disorder, the SUD would resolve itself.

Unfortunately, there is little consensus about the forms of “mental illness” that should be used to define the client with co-occurring disorders. It has been suggested that

coexisting conditions such as the SUDs and (1) anorexia, (2) bulimia, (3) gambling, (4) spousal abuse, (5) compulsive shopping, (6) compulsive sexual behaviors, (7) AIDS, and even (8) other physical disorders qualify as clients with co-occurring disorders (Minkoff, 2008). This text will limit this term to *coexisting* psychiatric disorders as defined by the American Psychiatric Association (2013) and an SUD. It is important to keep in mind that active substance misuse or the withdrawal from many drugs can simulate or magnify symptoms of psychiatric disorders (Buckley, 2006; Ross, 2008; Schuckit & Tapert, 2004). An excellent example of this is the anxiety often experienced by those with alcohol or benzodiazepine dependence during the withdrawal process. This anxiety is usually drug withdrawal-induced and will usually diminish or disappear entirely when the individual recovers from the withdrawal process or the effects of acute substance misuse, and thus do not qualify for the term co-occurring (Minkoff, 2008). An example of the patient with co-occurring disorders is the hypothetical patient with a bipolar disorder who also meets criteria for an AUD. Each disorder can influence the progression of the other, a fact that complicates the treatment of both conditions (Drake et al., 2001). This is clearly seen in the increased risk for suicidal behavior in patients with bipolar affective disorder who also have an alcohol use disorder (Oquendo et al., 2010). Either group has an increased risk of suicide, which is increased even further if the person has both a psychiatric problem and an SUD (Geppert & Minkoff, 2004; Mueser, Noordsy, Drake, & Fox, 2003; Ross, 2008; Sadock, Sadock, & Ruiz, 2015). Some estimate that those who misuse substances are 20 times more likely to commit suicide than those who do not misuse substances, and that up to 15% of those with an AUD commit suicide (Sadock et al., 2015).

Coexisting Substance Use and Medical Disorders

The example of a patient with hypertension and obesity offered as an example earlier in this section serves as an excellent example of how medical conditions can be intertwined. Sterling, Chi, and Hinman (2011) suggested that medical conditions and substance use disorders can also be intertwined, forming a distinct category of clients with co-occurring disorders. The individual’s substance use disorder could (a) cause a medical condition such as cirrhosis of the liver to develop, (b) exacerbate another medical disorder such as diabetes, or (c) increase the individual’s risk of exposure to certain diseases (Sterling et al., 2011). While this is an interesting perspective on coexisting medical and substance use issues, the main focus of this chapter will be on coexisting substance use disorders and mental illness.

¹This topic, like so many other topics in the addictions field, is worthy of a book in its own right. This chapter will attempt to review the more important issues in working with clients with co-occurring disorders.

Etiology of Co-Occurring Disorders

Torrens and Rossi (2015) reviewed the common hypotheses put forth regarding the relationship between SUDs and mental disorders. The first hypothesis was identified as SUDs and mental illness sharing risk factors that resulted in both (such as stressful experiences, trauma, or genetics). This is often called the “common factor model,” as noted by Mueser, Drake, and Wallach (1998) in their early review on models of etiology for co-occurring disorders. Torrens and Rossi noted the second hypothesis as the SUD causing neurological changes that then result in mental illness. Mueser and colleagues referred to this as the “secondary psychiatric disorder model,” in which the SUD is the causal factor for the development of the mental illness (Lieb, 2015). Note that this is not the same as symptoms caused because of current use or withdrawal from a substance. Ross (2008) identified that as a distinct model, in which the substance use would resolve when the primary condition is treated. This can certainly be challenging to ascertain, especially when the symptomology seems consistent with what can result from a substance (for example, panic symptoms that result from cocaine use; Ross, 2015). Instead, the secondary psychiatric disorder model proposes that changes that have occurred at a deeper level result in mental illness that would persist even if the SUD was treated and abstinence was maintained for some time. The third hypothesis put forth by Torrens and Rossi indicates that the SUD results from self-medication for the mental health symptomology; this is known as the secondary substance use disorder model (Mueser et al., 1998). Thus, the mental disorder is the causal link in the development of the SUD (Lieb, 2015). The fourth hypothesis presented by Torrens and Rossi is that the symptoms experienced by an individual are such that they appear as both an SUD and a mental disorder, but that the individual is misdiagnosed as having both because of a lack of information or incorrect assessment of symptomology. Ross (2015) uses an example of PCP-induced psychosis, which can continue for months after PCP discontinuance. In this case, the person could easily be misdiagnosed as having schizophrenia rather than substance-induced symptomology. In contrast, the fourth model put forth by Mueser and colleagues is often referred to as the “bidirectional model,” in that either can result in a greater susceptibility for the other, and that further interactional effects may continue to result over time. This may be considered by some as a “supersensitivity” to drugs for those with mental illness (Ross, 2008). It should be pointed out that no single hypotheses or model fully explains the problem of substance misuse by persons with mental illness. Ultimately, careful consideration of each individual and his or her use history, with careful timeline understanding, is

essential to considering whether any of these hypotheses is accurate for the person in question (Ross, 2015).

Clients with Co-Occurring Disorders: A Diagnostic Challenge

Clients with co-occurring disorders, or at least a client who may have co-occurring disorders, offers a challenge to health care professionals, as can be seen in considering the models presented above. The assessor must have “the ability to distinguish the signs and symptoms of the primary psychiatric illness from those caused or exacerbated by a primary SUD [substance use disorder]” (Geppert & Minkoff, 2004, p. 105). This is a daunting task. The majority of patients admitted to a substance treatment program will have symptoms of a psychiatric disorder at the time of admission. Many of these symptoms are substance-induced or withdrawal-induced, and will subside after a period of abstinence. The assessor might have to wait for as long as 2 to 8 weeks for the diagnostic picture to clear (Jones, Knutson, & Haines, 2004; Ross, 2008, 2015; Work Group on Substance Use Disorders, 2007). A careful clinical history might help differentiate substance-induced from actual psychiatric problems (Minkoff, 2008). For example, if an individual and family members attest that the depressive symptoms appeared months or even years before the individual started drinking heavily, it would be safe to assume that the observed symptoms of depression reflect a preexisting disorder that now coexists with the SUD. The depression is not substance-induced in spite of what might seem to be an apparent causal relationship. An accurate clinical history is thus of critical importance in the determination of actual dual diagnosis clients, as opposed to substance-induced psychiatric problems (Washton & Zweben, 2006). It is especially important to not utilize just a single source of information; instead, assessing with multiple sources of data is essential (Ross, 2015). In cases where the individual’s psychiatric symptoms are severe, the attending physician should immediately institute appropriate pharmacological treatment even if the symptoms are later determined to have been caused by a substance withdrawal syndrome (Busch, Weiss, & Najavits, 2005; Watkins, Burnam, Kung, & Paddock, 2001; Work Group on Substance Use Disorders, 2007). However, it should also be recognized that diagnosing a client with co-occurring disorders is an ongoing process, and might need to be modified as the patient recovers from the acute substance withdrawal.

Unfortunately, it is not uncommon for individuals who have the label of being a patient with co-occurring disorders to report that a careful clinical history was not carried out when they were admitted to a hospital or treatment center.

More than one patient has reported having been diagnosed as having a “transient psychosis” and started on antipsychotic medication without any health care professional inquiring about the individual’s possibly engaging in substance misuse. If the treating physician reaches for the prescription pad rather than spending a few more minutes to carry out a complete assessment, the person could potentially be exposed to potent medications without need. The diagnosis of a transient psychosis on his or her medical record is also a problem for the individual: Once a certain diagnosis is entered into a medical file, it is extremely difficult to have that diagnosis purged from the record, even if it was a mistake.

The accurate diagnosis of either an SUD or any form of mental illness is complicated by the fact that each condition is often viewed as a stigma (Pies, 2003). Where a hypothetical person with one condition or another might be motivated to use the defense mechanisms of denial and minimization, persons with co-occurring disorders frequently call upon these defenses to protect *both* their SUD and their mental illness (Minkoff, 2008; Shivani, Goldsmith, & Anthenelli, 2002). Forceful questioning about either the possibility that he or she has an SUD or a mental health problem may (a) cause the person to experience significant levels of shame or (b) awaken fears in the patient that by their admission to having a SUD they might lose entitlements (Social Security disability payments and health insurance benefits, for example). Some clients with co-occurring disorders fear that (c) their admission that they have an SUD could result in a refusal of access to psychiatric care, a fear that is not always unfounded. Finally, (d) because many clients with co-occurring disorders feel hopeless, they have little motivation to stop misusing the chemicals that bring them some degree of relief from their emotional pain.

As the material reviewed so far suggests, the diagnosis of a psychiatric disorder in an individual misusing substances, or the diagnosis of a substance use disorder in a psychiatric patient, can be extremely complicated. This raises the question that the next section attempts to answer.

Why Worry About Clients with Co-Occurring Disorders?

Perhaps the most eloquent answer to this question was provided by Geppert and Minkoff (2004), who suggested that:

As a whole this population has worse treatment outcomes, higher health care utilization; increased risk of violence, trauma, suicide, child abuse and neglect, and involvement in the criminal justice system; more medical comorbidity, particularly of

infectious diseases; and higher health care costs than people with a single disorder.

Geppert and Minkoff (2004, p. 103)

The increased risk of suicide in clients with co-occurring disorders has been estimated to be 60–120-fold higher than for the general population (Nielson et al., 1998). Further, clients with co-occurring disorders are at increased risk for incarceration, less able to handle personal finances, have a weaker support system, and are more prone to depression and feelings of hopelessness.

Although a person with both a substance use disorder and mental illness might not see the connection, clients with co-occurring disorders run the risk of exacerbating their psychiatric disorder through their misuse of recreational chemicals. This “sensitization” effect is especially noticeable in patients with schizophrenia (Ross, 2008). Even social use of alcohol, for example, can destabilize the client with co-occurring disorders and result in a greater need for rehospitalization (Mueser et al., 2003; Patrick, 2003; Prochaska, Gill, Hall, & Hall, 2005). Further, untreated psychiatric symptoms can serve as a relapse trigger for renewed substance misuse (Jones et al., 2004; Washton & Zweben, 2006). Clients with co-occurring disorders are also at increased risk of being assaulted and of being homeless (Brekke, Prindle, Woo Bae, & Long, 2001; Pankiewicz, 2008; Ross, 2008). They place an increased financial burden on society and often on their families by their need for repeated hospitalizations. Persons with co-occurring disorders are at increased risk for infections such as HIV, hepatitis C, and hepatitis B.² The treatment of all three conditions is often carried out at public expense, placing a hidden drain on social resources. Finally, persons with posttraumatic stress disorder (PTSD) have higher rates of substance use disorders, with up to two-thirds of those entering SUD treatment meeting criteria for PTSD (Mills et al., 2016), and they are at increased risk for re-traumatization (Mueser et al., 2003). Thus, there are significant social and personal financial losses either caused or exacerbated by substance use by psychiatric patients (Pankiewicz, 2008). All of these issues make the need to address co-occurring disorders undeniable.

Scope of the Problem

As many as 8.1 million individuals in the United States are thought to have a concurrent substance use disorder and mental illness problem (SAMHSA, 2016). Unfortunately, with the introduction of the first generation of antipsychotic

² These viral infections are discussed in Chapter 36.

medications in the late 1950s, society began to call for the “deinstitutionalization” of patients formerly hospitalized in private and state facilities.³ It was rationalized that agencies such as community mental health centers would provide appropriate treatment for these individuals. However, as the deinstitutionalization movement gained momentum, support services in the community were either overwhelmed or, as was found in many areas, simply did not exist. A complicating factor was that many formerly hospitalized individuals refused to take their prescribed medications following their release because of their harsh side effects. This often resulted in a “revolving door” at psychiatric facilities, where a person would be admitted for stabilization, discharged with a prescription(s) for his or her psychiatric disorder, would stop taking these medications because of their side effects, financial reasons, etc., decompensate, and require rehospitalization for stabilization.

However, the deinstitutionalization movement has achieved one of its goals: Many state psychiatric hospitals were closed, and in many cases the land was sold to private investors. An unforeseen side effect of this process is that at the start of the 21st century many persons who would have been sent to state hospitals in earlier generations are now homeless or incarcerated (Ross, 2008). Indeed, so many persons with mental illness are now incarcerated that some authorities view the prison system as the new state hospital system for the mentally ill.

Unfortunately, physicians are rarely trained to detect and treat SUDs in patients. Medical professionals’ training in SUDs in the first place is minimal, although it has improved according to some reports (National Center on Substance Abuse at Columbia University, 2000; Polydorou, Gunderson, & Levin, 2008). Other sources continue to note the inadequacies in medical training and continuing education (Davis & Carr, 2016). It has been found, for example, that emergency room physicians will, when confronted with a client with co-occurring disorders, commonly attribute the observed symptoms to the patient’s psychiatric disorder, to the exclusion of a possible SUD⁴ (Schanzer, First, Dominguez, Hasin, & Caton, 2006). In one study, only 24% of depressed

patients were even *assessed* for an alcohol use disorder by the attending physician (McDowell, Lineberry, & Bostwick, 2011). These facts underscore the need for training for health care professionals to better understand and properly diagnose patients with co-occurring disorders so that appropriate treatment referrals might be made. This would help correct the current situation, in which only 8% of clients with co-occurring disorders received treatment for both disorders, and 72% have never had both issues addressed in a treatment setting (Prochaska et al., 2005). Where treatment is offered, it is most often for either the mental illness problem or the SUD, but not both disorders (Buckley, 2006). In the correctional system, “treatment” is usually limited to pharmacological control of the mental illness problem alone, and it is a rare correctional system that provides pharmacological support for substance withdrawal.

If an individual has any form of mental illness, she or he is 270% more likely to have an SUD than the average person (Volpicelli, 2005). Various estimates suggest that between 30 and 80% of patients with a form of mental illness also have an SUD (Minkoff, 2008; Patrick, 2003; Roberts, 2004; Watkins et al., 2001). Table 25-1 summarizes the estimated concordance rate between the SUDs and various psychiatric disorders.

The relationship between a mental illness and a concurrent SUD is quite complex. There is evidence, for example, suggesting that the more serious the form of psychopathology, the more difficult it might be for the individual to abstain from drug misuse (Ritsher, Moos, & Finney, 2000).

TABLE 25-1 Estimated Concordance Rate Between Select Forms of Psychopathology and SUDs

Condition	Estimated Lifetime SUD Prevalence Rate
Depression	17–32%
Bipolar affective disorder	56–64%
Anxiety disorder	15–36%
Antisocial Personality disorder	84%
Attention deficit hyperactivity disorder (ADHD)	23%
Eating disorders: Anorexia	17%
Bulimia	46%
Posttraumatic stress disorder (PTSD)	30–75%
Schizophrenia	50%
Somatoform disorders	Unknown

SOURCE: Hartwell, Tolliver, and Brady (2009); Ross (2008); Ziedonis and Brady (1997).

³Whitaker (2010) argues convincingly that changes in federal reimbursement policies that shifted reimbursement for the mentally ill from state hospitals to nursing homes started the process of deinstitutionalization, and that the pharmaceutical industry took credit for this process.

⁴In defense of the attending physician, in many cases the emergency room doctor has limited historical data on the patient, who may be unable or unwilling to provide a history. This makes it difficult to differentiate between psychiatric dysfunction and substance-induced problems. However, it should also be noted that a misdiagnosis can have lifelong implications for the client (Schanzer et al., 2006).

This is consistent with the findings of Chambers and colleagues (2007), who concluded that rats that suffered damage to the amygdala region of the brain were more responsive to novel stimuli, less responsive to dangerous stimuli, and more prone to cocaine addiction. While suggestive, the assessment of amygdala function in the human brain is difficult, making it virtually impossible to determine whether this is a factor in human substance use disorders.

Psychopathology and Drug of Choice

For many years, clinicians were taught that there was a relationship between a patient's psychiatric disorder and his or her drug of choice. This hypothesis, although it continues to echo through the academic halls where health care professionals are trained, has not been strongly supported by the clinical literature (Drake, 2007; Drake & Mueser, 2002). Part of the confusion might be traced to the fact that much of the clinical data is drawn from research studies that perhaps unknowingly intermixed those who use substances and individuals who are *addicted* to a chemical(s) as participants. The spectrum of those who fit diagnostic criteria for an SUD is quite broad, which makes it challenging to interpret the data accurately. It has been assumed that those who misuse substances and those persons with severe SUDs and mental illness engage in substance misuse for the same reasons, an unsupported assumption at best. It is possible that an individual who meets the criteria for a mild SUD might engage in chemical use (possibly to self-medicate for emotional distress), whereas an individual with a mental illness who meets criteria for a severe SUD continues to misuse chemicals for other reasons (avoidance of withdrawal effects, association with a peer group, etc.) (Weiss, 2005). By intermixing participants from what may be the mild end of the SUD spectrum with those with a severe SUD and psychiatric condition(s), the results might have failed to find support for what is a seemingly very defensible hypothesis: that individuals who misuse substances seek to self-medicate their emotional pain by using alcohol and drugs. There are those who continue to work to measure what is a challenging hypothesis to investigate, such as Khantzian (2016) and Pesko and Baum (2016); thus we may find that this hypothesis will gain support in the future.

Proponents of the self-medication hypothesis often point to the apparent tendency for people who have developed posttraumatic stress disorder (PTSD) to engage in substance misuse (Cross & Ashley, 2007; Khantzian, 2003b; Preuss & Wong, 2000). This is a complicated matter, for the course of PTSD varies over time. The individual's goal in self-medication is also thought to vary over the course of

time, depending on whether he or she is facing the intrusive memories of the trauma or the emptiness of emotional numbing (Khantzian, 2003b). The self-medication hypothesis has significant appeal to clinicians because it seems to have face value; however, as noted above, the research has yet to draw conclusive support for this hypothesis. Perhaps some persons with mental illness are drawn to substance use for the same reason as other people: It is "cool" and a sign of rebellion (Sharp & Getz, 1998, p. 642). At the same time, substance misuse may offer the individual an identity of sorts, and, on some level, aid in the development of a social network (Busch et al., 2005; Drake & Mueser, 2002). Finally, in the minds of many clients with co-occurring disorders, the stigma associated with substance misuse is less severe than is that associated with mental illness, motivating many clients with co-occurring disorders to substitute the less severe stigma of having an SUD for that of mental illness (Sharp & Getz, 1998; Todd et al., 2004).

Individuals misusing substances, including those with some form of mental illness, tend to be more impulsive and interested in new sensations (Dervaux et al., 2001). This would suggest that individuals with a mental illness and an SUD might not be engaging in self-medication so much as seeking new sensory sensations for entertainment. This might also help to explain why cigarette smoking is two to three times more prevalent in persons with mental illness as it is in the general population (Kerr, Woods, Watson, & Hunter, 2013). A rarely considered variable is that the *availability* of alcohol or drugs influences an individual's substance use pattern (Drake, 2007). This hypothesis is supported by a study completed by Swartz and colleagues (2006), who concluded that the patterns of substance use by schizophrenic patients studied were similar to those found in the general community. A similar finding was reported by Lybrand and Caroff (2009), who observed that cocaine use by persons with schizophrenia was rare in rural areas of the country, but more common in urban areas where it is more easily obtained.

The factor of drug availability may have confounded early studies that attempted to find a correlation between the form of mental illness and the substance(s) being used. Most certainly there is little evidence to support a condition-specific pattern for substance use by those with mental illness and who also have an SUD, although Miles and colleagues (2003) *did* find a positive relationship between CNS stimulant misuse and violence. It is not clear whether the observed violence was the result of CNS stimulant misuse, which in itself can contribute to violent behavior by the individual using such substances, or the result of the individual's mental illness. Still, because the self-medication hypothesis has so many supporters, we will examine the relationship between various forms of mental illness and SUDs.

Attention Deficit Hyperactivity Disorder (ADHD)

In the final years of the 20th century, **ADHD** emerged from the depths of controversy to become an accepted diagnostic entity. Currently, it is thought that ADHD is estimated to be diagnosed in 7% of the population (Thomas, Sanders, Doust, Beller, & Glasziou, 2015).

A relationship between ADHD and substance use disorders was first suggested approximately two decades ago (Diller, 1998; Smith, Molina, & Pelham, 2002). For example, 21% of adults with ADHD are thought to have a concurrent cocaine use disorder (Acosta, Haller, & Schnoll, 2005). Both conditions are thought to reflect a dysfunction of the dopamine neurotransmission system of the brain (Sadock et al., 2015). There was a popular myth in the 1990s and the early part of the 21st century that adolescents with ADHD were at increased risk for CNS stimulant misuse in particular. The truth seems to be the opposite: *If* the adolescent's ADHD is adequately controlled, the individual appears to be at lower risk for the development of an SUD later in life (Work Group on Substance Use Disorders, 2007). However, it is still recommended that parents control access to the medication(s) being used to treat the ADHD to minimize potential misuse (Biederman et al., 2008; Knight, 2005). There does seem to be a risk for SUDs overall with a history of ADHD (Sadock et al., 2015), but it is not specific to a particular category of substances.

There is also increased risk for SUDs in children who suffer from one of the **conduct disorders**⁵ such as the **oppositional defiant disorder**⁶ (Sadock et al., 2015). These children do appear to be at increased risk for the development of an SUD in adulthood (August et al., 2006; Disney, Elkins, McGue, & Iacono, 1999; Lynskey & Hall, 2001). This apparent association between children with a conduct disorder and subsequent substance use might reflect the fact that between 35 and 50% of children diagnosed with ADHD also have a conduct disorder, and thus these findings are an artifact rather than a real clinical issue (Smucker & Hedayat, 2001).

There has been a great deal of research on childhood ADHD, and it has been discovered that in 65–85% of the cases, this condition does carry over into adulthood⁷ (Khurana & Schubiner, 2007; Sadock et al., 2015; Wilens, 2006). Between 15 and 25% of adults with ADHD will also

have an SUD at some point in their lives, and active substance misuse can make the diagnosis of ADHD difficult (Wilens, 2006). In cases of accurate diagnosis of adolescent ADHD, CNS stimulants such as methylphenidate or the amphetamines should *not* be the treatment of choice (Riggs, 2003). Rather, when there is a diagnosed or suspected SUD, medical professionals should choose compounds that have been found to be both safe and effective in treating ADHD without the high misuse potential of the CNS stimulants.⁸

There is preliminary evidence suggesting that individuals with ADHD are more vulnerable to the disinhibiting effects of alcohol than persons without ADHD (Weafer, Fillmore, & Milich, 2009). Adults with ADHD demonstrated less behavioral control in response to a given amount of alcohol than did control participants, and there was a dose-dependent loss of inhibition in both groups that was most pronounced in the ADHD group (Weafer et al., 2009). The authors of this study call for further research into this area, which hints that adolescents and adults with ADHD might not respond to alcohol in the same manner as normal persons will, possibly making them more vulnerable to alcohol use disorders.

New research is pointing toward a high prevalence of ADHD in those seeking treatment for cannabis use disorder (Notzon et al., 2016); thus, future research will continue to contribute to our understanding of the connection between SUDs and ADHD.

The issue of attention deficit hyperactivity disorder has been controversial, and the construct has even been challenged in the clinical literature. However, research using functional magnetic resonance imaging (fMRI) hints at abnormal regional brain activation patterns in adolescents and adults with ADHD as compared with age-matched normal clients (Cortese, 2012), suggesting that accurate tests to identify such patients can be developed in time. If such tests are developed, the client should be substance-free at the time of assessment, since these compounds can also cause abnormal regional brain activation patterns.

Schizophrenia

The relationship between **schizophrenia** and substance use disorders is rather complicated. To illustrate the problem, Jones, Lichtenstein, Grann, Långstrom, and Fazel (2011) suggested that individuals who have a preexisting alcohol use

⁵ See Glossary.

⁶ See Glossary.

⁷ Most substance rehabilitation professionals are not trained in the diagnosis of ADHD. Suspected cases should be assessed by a psychologist or physician who specializes in the diagnosis of such cases.

⁸ The clinician's suspicion that the patient might also have a concurrent SUD should be raised if the patient suggests that the *only* compounds that have worked for him or her are the CNS stimulants with higher misuse potentials.

disorder and who then go on to develop schizophrenia might not present with the same risk factors as do those individuals who develop an alcohol use disorder after developing schizophrenia. Further research in this area is clearly needed.

Research has shown that patients with schizophrenia have a 460% greater probability of developing a substance use disorder than the average person (Weiss, 2010). Expressed in other terms, between 40 and 70% of patients with schizophrenia have a concurrent SUD (Atkins, 2014; Lybrand & Caroff, 2009; Pankiewicz, 2008; Roberts, 2004). Statistically, the most commonly misused substance was nicotine, with between 70 and 90% of patients with schizophrenia also being cigarette smokers (Atkins, 2014; Pankiewicz, 2008). The second most commonly misused substance is alcohol, which is used by 34% of persons with schizophrenia (Jones et al., 2011). About 13% of persons with schizophrenia will develop a substance use disorder involving a compound other than alcohol (Ross, 2008).

Illicit substance use by patients with schizophrenia is associated with an earlier onset of schizophrenia, a poorer response to psychiatric treatment, higher rates of rehospitalization due to a resurgence of psychiatric symptoms, greater likelihood of being noncompliant with medications prescribed for the psychiatric disorder, and greater likelihood of engaging in suicidal behavior, being more violent, being victimized, being homeless, and being incarcerated than in schizophrenic patients who do not misuse recreational chemicals (Jones et al., 2011; Lybrand & Caroff, 2009; Pankiewicz, 2008; Weiss, 2010). A history of violent behavior in persons with a diagnosis of schizophrenia was found to be highly predictive of the later development of an AUD, often by a period of several years (Jones et al., 2011). Cannabis use has also been found to contribute to worsening psychosis in those with a schizophrenia diagnosis, and heavy use may be linked to the development of schizophrenia or earlier onset of symptomology (Sadock et al., 2015).

Higher-functioning patients with schizophrenia are thought to be more likely to have a concurrent SUD. Upon reflection, this becomes apparent: Because of their higher level of function, they perhaps have the interpersonal skills necessary to access alcohol or illicit drugs (Swartz et al., 2006). It should be pointed out that *availability* is a significant factor in the patient's substance use behaviors. Surprisingly, some patients with schizophrenia will seek out hallucinogenic compounds to use. Given that hallucinations are a primary symptom of schizophrenia, one would intuitively expect that patients with schizophrenia would avoid these compounds. However, many of these patients defend their use of hallucinogens because these compounds at least give them some degree of control over *when* they experience hallucinations, which provides an insight into their motivation to use these

compounds and the magnitude of emotional discomfort experienced by many patients with schizophrenia. Further, many persons with schizophrenia misuse alcohol or illicit drugs to provide relief from the side effects of the medications prescribed to treat their psychiatric disorder. Other persons with schizophrenia misuse alcohol or drugs to allow themselves a degree of control over when their psychiatric symptoms become active.

There is a significant interactional effect between schizophrenia and nicotine use disorder. As noted above, between 70 and 90% of patients with schizophrenia smoke cigarettes, and many are heavy cigarette smokers, smoking more than 40 cigarettes per day (Atkins, 2014; Pankiewicz, 2008). Fully 44% of all cigarettes consumed in the United States are consumed by persons with a mental illness, which exposes them to the dangers associated with cigarette smoking ("Why do the mentally ill die younger?", 2008). In the case of schizophrenia, it is thought that the nicotine in cigarettes helps to reverse many of the cognitive deficits associated with that disorder or the medications used to treat it (Pankiewicz, 2008). Persons who have both schizophrenia and a nicotine use disorder have twice the risk of heart disease and three times the risk of respiratory disease as nonsmokers (Kalman, 2010). Thus, the health risks associated with tobacco use mitigate any possible benefit from cigarette smoking in this population, and smoking cessation in this population is recommended (Hitsman, Moss, Montoya, & George, 2009).

It is interesting to observe that the cocaine withdrawal process is different for persons with schizophrenia than is normally seen (Carol, Smelson, Losonczy, & Ziedonis, 2001). Further, individuals who suffer from schizophrenia and who habitually use cocaine are at higher risk for developing **tardive dyskinesia**⁹ than those persons with schizophrenia who do not use this compound (Lybrand & Caroff, 2009). These disorders reflect a dysfunction of the dopamine neurotransmission system, and this might be why schizophrenic patients appear to experience more intense craving for cocaine than do non-schizophrenic patients during cocaine withdrawal. This suggests that there is a need for intensive intervention, including possible modification of medications to help these individuals cope with the symptoms of cocaine withdrawal.

There has been little formal research into the issue of which medications might be most effective in treating clients misusing substance and who also have a diagnosis of schizophrenia (San, Arranz, & Martinez-Rega, 2007). Anecdotal reports suggest that the "second-generation" or "atypical" antipsychotic medications are more effective in controlling the symptoms of schizophrenia in such patients than the older

⁹See Glossary.

medications used to treat this condition, but there has been little formal research into this area (San et al., 2007). However, new research is showing that integrative treatment does show long-term benefits for those with co-occurring SUDs and schizophrenia, a group that is often seen as hopeless (Drake & Green, 2015).

Anxiety Disorders

The relationship between SUDs and anxiety disorders is quite complicated (Maremmanni et al., 2010). Many of the drugs of misuse can induce anxiety either as a side effect when they are being used or during the withdrawal process. The amphetamines and marijuana are examples of the former, while alcohol is a prototypical example of the latter. Thus, it is imperative that the health care professional(s) working with an individual determine whether he or she is experiencing substance-related or substance withdrawal anxiety, or if they have a concurrent anxiety disorder, to assist in the proper treatment of the patient. The team of Kushner, Specker, and Maurer (2011) observed that the term “anxiety” is too inclusive, as different forms of anxiety disorders have different risk levels for substance use disorders. Approximately 10.4% of persons with a **generalized anxiety disorder** were found to have misused a drug in the preceding 12 months, for example, but only 3.8% of persons with a **specific phobia** had done so (Kushner et al., 2011).

One point that assists in the differentiation between substance-induced versus anxiety is that anxiety disorders are generally thought to predate the development of the substance use disorder (Cheng, Gau, Chen, Chang, & Chang, 2004). Thus, a wise clinician will carefully diagnose based on history reported by the individual as well as information from other sources. However, Kushner and colleagues (2011) challenged this belief, noting that in approximately half of the cases where a person has a concurrent SUD and an anxiety disorder, the latter developed *after* the substance use disorder. The authors supported this claim with the observation that pathological substance use exacerbated preexisting anxiety symptoms. These observations do underscore the need for a case-by-case evaluation to determine the exact relationship between the individual’s anxiety disorder and her or his SUD.

The anxiety disorders, at least in theory, provide a clear example of the self-medication hypothesis (Khantzian, 2003b), especially if one is to consider research like that of Cheng et al. (2004), discussed above. Hypothetically, the individual would be drawn to the misuse of alcohol, opioids, or benzodiazepines, all compounds with an anxiolytic effect, to self-medicate their anxiety. This theory is supported by research finding that up to 50% of those persons with

a generalized anxiety disorder (GAD) will also have some form of a SUD (Alegria et al., 2010).¹⁰ But, as noted above and in earlier sections, this does not mean that this is accurate for all individuals. Careful consideration of the individual is necessary.

There are a number of effective medications as well as psychotherapies for persons who suffer from some form of anxiety. However, some medications are contraindicated for use with individuals misusing substances who also have an anxiety disorder. For example, although the monoamine oxidase inhibitors (MAOIs) have been found to be very effective in treating **social anxiety disorder**, these medications are contraindicated for patients with an SUD because of the risk that the patient will develop a potentially fatal hypertensive crisis as the MAOI interacts with some of the compounds found in beer, wine, and liquor (Book & Randall, 2002). Further, while the benzodiazepines have been found to be useful for short-term relief of anxiety, their misuse potential prohibits their use in treating patients with an anxiety disorder and a concurrent substance use disorder (Jones et al., 2004; Riggs, 2003). The selective serotonin reuptake inhibitors (SSRIs) are now viewed as the most appropriate treatment for these individuals (Book & Randall, 2002; Jones et al., 2004; Ross, 2008). Buspirone has also been found to be helpful in many cases of generalized anxiety disorder (Virani, Bezchlibnyk-Butler, & Jeffries, 2009), while “beta blockers” have been found useful in specific cases. Kushner and colleagues (2011) also observed that pharmacotherapy should not be the only treatment utilized, but that an integrated team approach would be most effective.

The Dissociative Disorders

The **dissociative disorders** represent a series of related conditions in which the individual essentially is able to “detach” from reality for periods of time to escape from extreme psychological stress. One man, upon being told of the death of his spouse, recalls the sensation of watching himself from across the room as he lost consciousness and hit his head against a concrete wall and a cement floor before coming to rest, all the while thinking “that’s gonna hurt.” This short period of dissociation illustrates how dissociation can help the person escape from psychological stress, although the man in this case was the first to admit that the emotional numbing did not last long enough.

¹⁰This study refers to *lifetime* prevalence rate, where Kushner et al. (2011) only spoke of anxiety-disordered persons who had misused a drug in the previous 12 months. This accounts for the discrepancy between the figures used by each set of authors.

It should be noted that dissociation does not involve the use of psychoactive chemicals with these individuals. This state is achieved by the mind itself. In its most extreme form, the individual might manifest more than one personality, a condition that was once called “multiple personality disorder” and is now called **dissociative identity disorder** (DID). Approximately one-third of patients with DID have a coexisting SUD (Putnam, 1989). CNS depressants such as alcohol or the benzodiazepines are the substances most commonly misused by patients with DID, although on rare occasions the CNS stimulants are also misused (Putnam, 1989). Hallucinogens do not seem to be a popular class of drugs to be misused for this subpopulation, for unknown reasons (Putnam, 1989). Substance use by patients with DID does tentatively appear to fit the self-medication hypothesis discussed elsewhere in this text (Putnam, 1989). It does appear that there may be differences between the “normal” patient with an SUD and a patient with a coexisting DID and SUD. The latter group of patients usually do not report reduced discomfort at the end of detoxification, but may report continued distress, or even higher levels of distress, following detoxification (Putnam, 1989). The reasons for this are not known at the present time, and with reduced interest in this diagnosis, research may not be forthcoming in the future (Paris, 2012).

Obsessive-Compulsive Disorder (OCD)

Obsessive-compulsive disorder is the fourth most common psychiatric disorder found in the United States (Sadock et al., 2015). Researchers disagree about the percentage of patients with OCD who have a concurrent substance use disorder. Encrenaz and colleagues (2009) offered an estimate of 11.5% of men and 5.5% of women, with persons with OCD having a concurrent SUD. Drawing on another sample, Goldsmith and Garlapati (2004) estimated that up to 36% of those persons with OCD will have a concurrent SUD. There does not appear to be a specific compound favored by individuals with OCD, although theoretically patients with OCD might be drawn to the CNS depressants such as alcohol or the benzodiazepines because of their anxiolytic properties. It is certainly important to realize that OCD symptomology is often seen in those who have taken high doses of stimulants (Sadock et al., 2015); thus, once again, careful consideration of substance use by the clinician is important in distinguishing OCD from stimulant-induced OCD.

Bipolar Affective Disorders

The **bipolar affective disorders**, or what was once called *manic-depression*, represent a complicated set of interlocking conditions that are still not clearly understood by clinicians.

These disorders are “characterized by disabling and sustained mood swings (mania, hypomania, and depression)” (Atkins, 2014, p. 155). Alcohol misuse by persons with a bipolar disorder is associated with poor medication compliance, increased functional impairment, and possibly increased risk of suicide (Goulding & Fleming, 2011). The manifestations of this disorder can be exacerbated by the misuse of compounds such as the amphetamines, alcohol, and cannabis (Maremmanni et al., 2010). Further, the process of withdrawing from the various drugs of misuse can induce either mania or depression even in the normal person, and for the individual with a bipolar disorder, the process of withdrawal can exacerbate the individual’s preexisting psychiatric distress (Sonne & Brady, 2002; Suppes & Keck, 2005).

It has been estimated that between 40 and 70% of patients with a bipolar disorder will also demonstrate symptoms of a substance use disorder at some point in their lives (Atkins, 2014; Brown, 2005; Nery & Soares, 2011; Ostacher & Sachs, 2006; Tolliver, 2010). Substance misuse by patients with co-occurring disorders appears to be a factor in the need for more frequent hospitalizations, less effective symptom control, and an increased failure rate for therapeutic intervention for either condition (Maremmanni et al., 2010; Nery & Soares, 2011; Sadock et al., 2015; Tolliver, 2010). One reason for the increased rate of treatment failure is the possibility that the sense of confidence and enthusiasm often seen during the manic stage is often interpreted by rehabilitation center staff as treatment progress rather than a symptom of mania (Maremmanni et al., 2010).

Clinical research suggests that those with a bipolar disorder who also misuse substances tend to use more drugs during the manic phase of their condition, although an exception to this rule is the alcoholic with a bipolar affective disorder (Maremmanni et al., 2010). It has been hypothesized that some patients might use CNS stimulants such as cocaine to simulate the manic phase of a bipolar disorder to prolong the sense of power and invulnerability experienced during the earlier phases of mania. In contrast, persons with an AUD who are in the depressed phase of a bipolar disorder drink more than they do at other times, possibly in an attempt to “numb” themselves to their emotional pain (Maremmanni et al., 2010).

Persons with concurrent bipolar and substance use disorders are also at high risk for other psychiatric problems such as generalized anxiety disorder, panic disorder, and posttraumatic stress disorder. For reasons that are not known, persons with a concurrent bipolar affective disorder and substance use disorder are also five times as likely to contract the hepatitis C virus¹¹ as persons who do not suffer from

¹¹ Discussed in Chapter 36.

a bipolar disorder (Tolliver, 2010). One possible explanation is that persons in the manic phase are more likely to engage in high-risk behaviors, exposing themselves to the virus more often than the average person.

In the person with co-occurring bipolar and SUD, the depression that is often induced by the withdrawal process might serve as a relapse trigger¹² (Weiss, 2005). To complicate matters, persons with a concurrent bipolar disorder and SUD are likely to deny their illness, making accurate diagnosis impossible (Tolliver, 2010). It is imperative that the clinician have an *accurate* clinical history to help determine whether the observed symptoms predate or postdate the patient starting to misuse chemicals (Minkoff, 2008). Collateral information is often of value during the formulation of a differential diagnosis and treatment approaches (Minkoff, 2008; Ostacher & Sachs, 2006). Pharmacological treatment often involves the use of mood-stabilizing medications, which have been proven to be safe and effective in the treatment of bipolar disorders (Maremmanni et al., 2010). Unfortunately, there are few treatment guidelines for working with the person with a concurrent bipolar affective disorder and SUD, and pharmacotherapy¹³ must be carefully initiated and monitored to ensure optimal response to the pharmaceuticals being used to treat both disorders.

Depression

The experience of depression, especially major depression, which affects approximately 15 million in this country (Horstman, 2010), is one of profound sorrow, pain, hopelessness, and despair. Research has shown that depressed individuals are at increased risk for the development of an SUD: 21% of those who have experienced depression in the last year also have an alcohol use disorder, and 9% met the diagnostic criteria for a drug use disorder (Wells, Paddock, Zhang, & Wells, 2006). Over the course of their lifetime, up to 40% of patients with a major depression, and 31–43% of patients with dysthymia, will also have an SUD (Evans & Sullivan, 2001; Goldsmith & Garlapati, 2004; McIlveen, Mullaney, Weiner, Diaz, & Horton, 2007; Sadock et al., 2015). There is a marked gender gap between men and women with depression: 14% of men who are depressed also have a SUD, as opposed to just 5.8% of depressed women (Encrenaz et al., 2009). This discrepancy might reflect the tendency for women to seek professional help with depression more often than do men.

There is a strong financial incentive to identify and effectively treat patients with concurrent depression and SUDs.

The amount of money spent treating patients with comorbid dysthymia and an SUD was *five times* higher than that necessary to treat a patient with only an SUD (Westermeyer, Eames, & Nugent, 1998). Further, untreated depression is a possible relapse trigger following detoxification for patients with comorbid depression and SUDs (McIlveen et al., 2007; Nunes & Levin, 2006). Although clinical lore holds that persons with alcohol use disorders are more prone to major depression, a more common pattern is that individuals with major depression are at increased risk for the development of an alcohol use disorder (Fergusson, Boden, & Horwood, 2009). Unfortunately, the treatment of concurrent depression and substance misuse is rather complicated in that the use of chemicals in this patient population can either exacerbate their depression or negate the effects of prescribed medications that are designed to help treat their depression. The reverse is also true: Untreated depression complicates the treatment of the SUDs (Wells et al., 2006).

To identify individuals with a primary depression,¹⁴ it is necessary to obtain a detailed, comprehensive psychiatric history (Minkoff, 2008; Nunes & Levin, 2006; Ross, 2015). This history will reveal whether the depression predated the SUD, or developed after the individual began to misuse chemicals. However, in cases where the individual has a long-standing SUD, this differentiation might not be possible. In all cases, the SUD should be addressed immediately, while the health care professionals continuously monitor the patient's status against the possibility that she or he has a primary depression that might have been masked by the SUD (Minkoff, 2008).

Eating Disorders

Although **eating disorders** are predominantly found in girls, adolescent girls, or women, there is a small subgroup of men who also have one form of eating disorder or another.¹⁵ There is a known relationship between eating disorders and alcohol use disorders, and each complicates the treatment of the other (Cohen & Gordon, 2009). Rates of eating disorders in those seeking SUD treatment are said to be around 35%, whereas the rate of eating disorders in the general public is around 3% (Elmqvist, Shorey, Anderson, Temple, & Stuart, 2016). The relationship between eating disorders and the other forms of drug use is not as clear at this time, although Fouladi and colleagues (2015) found that those with bulimia

¹² Discussed in Chapter 34.

¹³ Discussed in Chapter 33.

¹⁴ As opposed to a substance-induced depression.

¹⁵ There are several subtypes of eating disorders. The topic of eating disorders and the recognition of each subtype is beyond the scope of this text. The reader is referred to any of a growing number of books on the topic of eating disorders for more information.

nervosa were more likely to misuse alcohol and other drugs than those with other eating disorders (such as anorexia and binge eating disorder). They also found that more frequent bingeing and purging in any of the study participants did point toward higher substance use (Fouladi et al., 2015). It is known that persons with an eating disorder often use alcohol to suppress their appetite, or to avoid or suppress food “urges” (Cohen & Gordon, 2009). Since many of the other drugs of misuse suppress appetite or make the user numb to the sensation of hunger, it is not unreasonable to expect that some persons with an eating disorder use these compounds for the same reasons.

It has been suggested that eating disorders are a form of self-medication for emotional distress, although this theory has not met with universal acceptance (Cohen & Gordon, 2009). It has also been suggested that alcohol use disorders and eating disorders are different manifestations of a self-regulatory mechanism(s), although the exact causal mechanisms for either condition remain uncertain. It has been found that less than 20% of publicly funded substance use rehabilitation programs screen for eating disorders, and that only a small percentage of treatment programs have the ability to treat persons with co-occurring eating disorders and substance use disorders (Cohen & Gordon, 2009). The rate of failure to complete treatment is of significant concern, with Elmquist and colleagues’ (2016) preliminary findings highlighting that the presence of eating-disordered symptomatology results in greater rejection of treatment. As should be obvious by now, there is much to be discovered about the relationship between eating disorders and substance use disorders, as well as the treatment of these conditions when they are both found in the same person.

Compulsive Gambling

Gambling is a “behavioral addiction” that is in itself not a sign of psychopathology. The vast majority of the population will gamble at one time or another, even if the stakes are as small as the cost of a can of soda. However, about 2–7% of those who gamble do so compulsively, placing them at risk for a wide range of psychosocial and possibly legal problems (Grant, Kushner, & Kim, 2002; Nordstrom & Williams, 2012; Potenza, Fiellin, Heninger, Rounsaville, & Mazure, 2002). Further, there is a significant overlap between the SUDs and **compulsive gambling**. Compulsive gamblers are thought to be two to four times as likely to have an alcohol use disorder as the average person (Grant et al., 2002), and 44% of compulsive gamblers will admit to an alcohol use disorder at some point in their lives (Grant et al., 2002). More recent research indicates that the overlap of AUDs and compulsive gambling may be as much as 73% over one’s lifetime,

with other SUDs being up to 38% (Rash, Weinstock, & Van Patten, 2016). Both disorders can initiate the reward cascade in the brain. Once initiated, the reward cascade potentially can become a relapse trigger for the other disorder.

A popular belief is that the negative experiences (financial losses) incurred while gambling entice the individual to use chemicals to make themselves numb to the emotional pain of their financial distress. Surprisingly, there is little correlation between the amount of money lost and the intensity of the individual’s depression (Unwin, Davis, & De Leeuw, 2000). If the individual has lost a significant amount of money, then there is a danger of suicidal thinking, if not suicide attempts by the client. Long-term rehabilitation involves confronting the individual’s irrational beliefs about both substance use and gambling, and helping the gambler develop a coping style to address both problems. Self-help groups such as Gambler’s Anonymous (GA), modeled after similar groups for alcohol and other drugs, are often of value in this effort. However, clinicians must keep in mind that compulsive gambling disorders frequently coexist with substance use disorders, and that each condition can complicate the treatment of the other.

Personality Disorders

It has been estimated that 50–60% of clients with an SUD have a concurrent **personality disorder**¹⁶ (Work Group on Substance Use Disorders, 2007). Individuals with a personality disorder and an SUD are over-represented in the population of patients with SUDs (Atkins, 2014; Echeburua, de Medina, & Aizpiri, 2005). The authors concluded that 40% of individuals with an alcohol use disorder also met the diagnostic criteria for a personality disorder, but only 6% of the control sample were found to have a personality disorder (Echeburua et al., 2005). The most common subgroup were those individuals with a dependent personality disorder (13% of their research sample), followed by the paranoid personality disorder and the compulsive personality disorder (10% each), according to the authors. Others indicate that borderline personality disorder and antisocial personality disorder show greater prevalence in those with SUDs (Atkins, 2014). The discrepancy in these prevalence statistics may relate to the different research methods, whether the focus is on those within treatment or not, as Atkins (2014) indicated that those with borderline and antisocial personality disorders are most likely to seek out treatment, and thus would be over-represented in research focused on treatment settings.

¹⁶To learn more about the concept of personality disorders, the reader is referred to the *DSM-5* (American Psychiatric Association, 2013) or a good psychopathology textbook.

TABLE 25-2 Subgroups of Antisocial Disordered Clients

Subgroup	Percentage of Total Sample	Conduct Disorder in Childhood?	Characteristics
Early onset, strong ASPD features	10	Yes	Meets criteria for diagnosis of ASPD
Late onset, strong ASPD features	12	Yes, but not as often as the above group	Antisocial personality disorder symptoms do not appear until adulthood; individual will have only minor childhood behavioral problems
Emotionally unstable ASPD subgroup	18	Moderate history of childhood conduct disorder	Hostility, guilt, dependent behaviors, avoidant features all begin to manifest in adulthood
Non ASPD/substance-induced features	17	Rarely	Substance-induced ASPD features
Moderate substance misuse/moderate ASPD features	15	Rarely	ASPD features intermixed with low levels of guilt or depression and some substance-induced distress
Low ASPD	28	Rarely	Rare reports of antisocial behaviors in adulthood

SOURCE: Based on Alterman et al. (1998).

Antisocial Personality Disorder and Substance Use Disorders¹⁷

It has been estimated that between 15 and 50% of men and 1% of women with an AUD have a concurrent personality disorder. Clinical lore maintains that the most common and certainly most difficult of these is the **antisocial personality disorder** (ASPD) (McCraday, 2001; Shivani et al., 2002), and, as noted above, those with personality disorders may be most likely to seek out treatment for a co-occurring SUD. Over the course of their lives, just under 6% of the men and 1.2% of the women will meet the diagnostic criteria for ASPD (Daghestani, Dinwiddie, & Hardy, 2001). There is a great deal of overlap between ASPD and SUDs. This single personality disorder accounts for 23% of the overlap between personality-disordered clients and substance-abusing clients (Grekin, Sher, & Wood, 2006). Persons with ASPD who experiment with alcohol or illicit drugs have been found to engage in substance misuse at an earlier age,

and are 21 times as likely to have an alcohol use disorder as the average person (Moeller & Dougherty, 2001; Mueser et al., 2003). Nor is the overlap limited to the AUDs: Up to 48% of those individuals with a cocaine use disorder, 48% of those with an opiate use disorder, and 62% of polydrug users have ASPD (Vaglum, 2003).

Alterman and colleagues (1998) examined the relationship between antisocial personality disorder and opioid use disorders, and found that in their sample of 252 individuals in a methadone maintenance program diagnosed with ASPD there were six subgroups of patients, as described in Table 25-2. As noted in the table, for at least some persons the observed ASPD features may be a reflection of a substance-induced condition rather than a true personality disorder (Alterman et al., 1998; Evans & Sullivan, 2001). The lifestyle imposed on the individual by substance misuse may induce what at first glance appears to be an antisocial personality disorder. Such individuals might be viewed as having an “acquired” personality disorder. Unlike persons with true ASPD, such individuals experience psychiatric distress such as anxiety and/or depression, and might be able to benefit from substance use rehabilitation programs (Evans & Sullivan, 2001; Modesto-Lowe & Kranzler, 1999).

Borderline Personality Disorder and SUDs

The **borderline personality disorder** is often an enigma to both the mental health professional and the layperson. Clinically, individuals with BPD alternate between

¹⁷ MacKenzie (2012) observed that 25% of the population has evidence of exposure to toxoplasma, a parasite that usually infects cats and mice. In humans this parasite can cause increased recklessness and reduced conscientiousness, both of which are characteristic of persons with the antisocial personality disorder. Flegr (quoted in Walters, 2013) provided preliminary evidence that infection with this parasite can influence human behavior. This raises questions in the mind of the author about the possibility of a relationship between toxoplasma infection and ASPD, as well as a possible relationship between toxoplasma infection and substance use disorders. These observations are speculative on the part of the author, but are worthy of consideration.

over-idealization of significant others and total rejection and distrust of the same person after a perceived slight or rejection.¹⁸ They do, however, share the characteristics of impulsiveness and overemphasis on their own perceived “rights,” as does the client with antisocial personality disorder, and are often misdiagnosed as having ASPD. Perhaps 30–50% of persons with a SUD will also have BPD (Work Group on Substance Use Disorders, 2007). The role of the chemical(s) varies from person to person with BPD, but for many, alcohol or drugs help to calm the emotional fires within or distract them from their emotional pain. Substance use rehabilitation for persons with this disorder is often difficult and labor-intensive, requiring a commitment on the part of the therapist to continue to work with the client, possibly for as long as a decade or more.¹⁹

Mixed Personality Disorders

Very few individuals present a “pure” personality disorder in which their personality type meets the diagnostic criteria for *only* one of the many personality disorders. Most individuals with personality disorder features present symptoms from two or more personality subtypes, although primarily from one personality type. A hypothetical person with histrionic personality disorder might have some antisocial personality disorder traits, and possibly some compulsive personality traits, to cite one possible pattern. Experienced clinicians usually have seen many different combinations of personality traits intermixed in substance-misusing clients.

Co-Occurring Disorders/ Victimization Issues

There is a significant overlap between SUDs and a history of past or current victimization²⁰ (Carr & Szymanski, 2011; Smith, Homish, Leonard, & Cornelius, 2012). Such patients present a therapeutic dilemma to substance rehabilitation professionals. While it is thought to be necessary for individuals to come to terms with their abuse history as part of their recovery program (Cohen, 2000; Sinha, 2000), most programs lack the resources, time, or treatment staff with

sufficient training to help the individual address this issue (Blum, 1998; Cohen & Hien, 2006).

It is a mistake to assume that the victimization *caused* the SUD. Such a viewpoint reflects *post hoc, ergo propter hoc* (“after this, therefore because of this”) reasoning (Lilienfeld, Lunn, Ruscio, & Beyerstein, 2010). This is not to deny that sexual abuse causes emotional suffering, but the theory that childhood sexual abuse *causes* personality changes or substance use disorders later in life is not currently supported by the clinical literature.²¹ In some cases, the SUD preceded the individual’s victimization (Brook, Pahl, & Rubenstone, 2008). Because there are many factors that can cause or exacerbate an SUD, professionals working with such individuals must carefully assess the relationship between the individual’s SUD and victimization. This further underscores the need for gender-specific treatment programs. Women who have been victimized by a male might feel inhibited in a mixed group setting (McCrady, 2001). Further, the language used by many men in treatment is often offensive, if not demeaning, to women, contributing to a higher dropout rate for women in mixed group settings as opposed to gender-specific programs. Further, traditional substance rehabilitation programs, following the example set by 12-step programs such as Alcoholics Anonymous,²² place great emphasis on surrender and submission. Women with victimization issues find this to be difficult, if not impossible, to accept.

Posttraumatic Stress Disorder

While not all forms of physical or sexual abuse result in the development of posttraumatic stress disorder (PTSD),²³ there does appear to be a relationship between substance use disorders and exposure to situations that can induce PTSD. As is true for many forms of psychological distress, there is a marked discrepancy between the percentage of men and of women who develop this disorder. Women appear to develop PTSD about twice as often as men (Najavits, 2010). While 20% of men misusing substances report having experienced some form of serious sexual, physical, or emotional trauma, between 30 and 60% of women misusing substances report

¹⁸ A therapist arriving 5 minutes late for a session might serve as sufficient provocation for a person with BPD to mistrust others, for example.

¹⁹ The author has found that the *Addiction Treatment Planner* by Robert R. Perkinson, Arthur E. Jongsma Jr., and Timothy J. Bruce provides many useful treatment goals for the counselor with a client with BPD.

²⁰ The reader should keep in mind that men are at times the *victim* of abuse and *not* the perpetrator. Male victims of abusive relationships are often reluctant to step forward because this is not consistent with social role expectations that the man should be able to defend himself, especially from a female aggressor.

²¹ This theory is commonly repeated in “pop” psychology and self-help books, and appears to survive because (a) it has been repeated so often that people come to believe it must be true (or why would people still be saying it?), and (b) it is a simplistic answer to a social problem.

²² Discussed in Chapter 35.

²³ The topic of posttraumatic stress disorder (PTSD) is very complex and lies outside the scope of this text. The reader is referred to Sadock et al. (2015) for more information about PTSD.

having suffered through such life experiences (Finnegan & Kandall, 2008; Ross, 2008). Gielen, Krumeich, Tekelenburg, Nederkoorn, and Havermans (2016) noted that those with co-occurring SUDs and PTSD do not start use because of their trauma history, but that the symptoms related to trauma are connected to the continuation of substance misuse.

Thus, the individual who suffers from PTSD presents a difficult challenge to those providing treatment. The adaptive mechanisms seen in PTSD often are interpreted by the individual as evidence that they are losing their mind and often make others uncomfortable. For example, the exaggerated startle reaction often seen in persons with PTSD is not a sign that they are losing their mind, but a common reaction to traumatic experiences. Clients who have been exposed to interpersonal violence (IPV) frequently have post-assault distrust of others, presenting an additional challenge to rehabilitation professionals. Those with PTSD often turn to alcohol or illicit drugs to self-medicate their intrusive thoughts about the traumatic event, emotional “numbing,” nightmares, and mood swings.²⁴ Unfortunately, the individual’s substance use disorder might predate the development of PTSD or even be a precipitating factor in the traumatic event that forms the core of PTSD.²⁵

Systematic research into the percentage of patients with PTSD who attempt self-medication through the use of alcohol and illicit drugs is lacking. However, the team of Simpson, Stappenbeck, Varra, Moore, and Kaysen (2012) did find a relationship between the individual’s experience of PTSD symptoms and alcohol use in their research participants. The authors found that those who experienced PTSD-induced exaggerated startle responses and increased anger and irritability were most likely to experience same-day craving for alcohol, while persons who experienced PTSD-related nightmares, emotional numbing, and PTSD-related hypervigilance were more likely to crave alcohol the next day.

Pharmacotherapy with clients with PTSD is difficult. The benzodiazepines are thought to either have no effect on posttraumatic anxiety or possibly even contribute to the development of posttraumatic anxiety because of the dissociative effect induced by this class of medications (Shalev, 2009). Generally, the SSRIs are the first consideration for treating PTSD (Sadock et al., 2015). Cognitive-behavioral therapies (CBT), possibly combined with relaxation training

and coping skills training, has shown promise in assisting individuals with PTSD; however, research evidence for the effectiveness of such interventions is mixed (Shalev, 2009). A treatment team approach might offer some promise in working with these individuals, especially since research suggests that if therapists focus only on the SUD, it is unlikely that the patient will experience much relief from his or her PTSD symptoms (Najavits, 2010).

The loss of hope in PTSD is one of the more damaging aspects of this disorder; thus, establishing one therapeutic goal at a time for the client at the outset of therapy may be important (Najavits, 2010). However, in spite of these insights into the nature of PTSD and possible treatment approaches to help the client come to terms with past trauma, these clients will continue to present unique challenges to health care professionals, who should keep abreast of the latest developments in PTSD treatment to be able to assist their clients.

Problems in Working with the Client with Co-Occurring Disorders

The client with co-occurring disorders is often difficult to work with. Their motivation for substance rehabilitation will vary from individual to individual, but as a group they tend to request substance treatment only as a result of personal, family, or legal problems (Goldsmith & Garlapati, 2004). Often they present with combinations of problems. Unfortunately, treatment resources (such as dedicated treatment programs for clients with co-occurring disorders, financial support for treatment, etc.) are woefully scarce (Pepper, 2004; Priester et al., 2016). Clients with co-occurring disorders frequently have fragile support systems, and 12-step support groups frequently are intolerant of the special needs of this population of persons. For example, many 12-step support groups view the use of *any* prescribed mood-altering medications as an indication that the client is substituting one addiction for another (Evans & Sullivan, 2001). Further, these clients often feel out of place in 12-step groups, especially in the earlier stages of rehabilitation (Petrakis, Gonzalez, Rosenheck & Krystal, 2002). Thankfully, there is a move to establish “double trouble” or co-occurring disorder 12-step support groups in many communities.

Many clients with co-occurring disorders demonstrate a special form of denial that can be called (for want of a better term) **free-floating denial** or **interchangeable denial**. This form of denial involves the utilization of one problem to defend the other. Thus, if a health care professional should attempt to focus attention on a psychiatric condition, the

²⁴The reader is referred to the current edition of the *Diagnostic and Statistical Manual of Mental Disorders* for a full listing of the diagnostic criteria for this condition.

²⁵The individual’s misuse of alcohol and/or illicit drugs might make them more vulnerable to being victimized, or lower inhibitions sufficiently that the individual then engages in violent behaviors that are atypical for them.

patient will express a desire to talk about their SUD. If a substance rehabilitation professional should attempt to address the SUD, the client will talk about his or her mental illness issues. A variation of this process is when patients with a dissociative identity disorder attribute their loss of memory (experienced when one personality is forced out of the seat of consciousness so that another might take over) to chemicals rather than to the process of dissociation.

To complicate matters, many health care professionals view clients with co-occurring disorders as being primarily substance-misusing patients who require substance treatment. At the same time, many substance treatment professionals view the same individuals as psychiatric patients. The deplorable outcome of this professional blindness is that the patient might be bounced between chemical dependency and psychiatric treatment programs (Minkoff, 2008). This is a legacy of the federal drug treatment initiatives of the 1970s and 1980s, which established a number of different agencies focused on the identification and rehabilitation of individuals who misuse substances (Osher & Drake, 1996). Responsibility for supervision and development of psychiatric treatment programs was assigned to a different series of federal agencies, and for the most part interdepartmental communication and cooperation was virtually nonexistent.²⁶ As a result of this process, it is the rare staff psychiatrist in a treatment facility who understands that intense emotions generated by psychiatric distress can serve as relapse triggers for the patient with co-occurring disorders (Goldsmith & Garlapati, 2004). Further, in their efforts to ease the client's distress, the attending physician might administer potentially addictive compounds to the client, with the best of intentions but with little insight into how these compounds might complicate the individual's recovery from his or her SUD.

Traumatic Brain Injury and SUDs²⁷

The term **traumatic brain injury** (TBI) is a nebulous term often used synonymously with the terms *head trauma* or *head injury*. Currently, the abbreviation TBI is used to identify *all* possible injuries to the brain that may be found in the person who has experienced injury to the brain. The term *head trauma* is *not* synonymous with traumatic brain injury. By definition, TBIs are a subset of head injuries, specifically reserved for events that cause injury to the tissues of the

brain. Such injuries exist on a continuum from very mild to life-threatening. In addition, what initially appeared to be a mild TBI could, with the passage of time, prove to be life-threatening. The outcome of a TBI can range from complete recovery, to permanent disability, to the death of the victim.

Physicians often assess the severity of a TBI using the Glasgow Coma Scale (GCS), which attempts to measure the individual's level of consciousness on a scale of 3 to 15. The individual's ability to respond to verbal commands ("open your eyes!"), to engage in voluntary movement ("move your left hand!"), and to provide information ("What is your name?") are rated. Lower scores reflect more severe traumatic brain injuries, since the individual would be unable to respond to the verbal commands. TBIs are then classified as mild (GCS scores of 13–15), moderate (GCS scores of 9–12), or severe (GCS scores of 3–8). In spite of its widespread use, the GCS score has only a limited ability to predict ultimate outcomes.

By this point the student is starting to wonder why all of this information is of importance in a text on substance use disorders. The answer is simple: Persons with substance use disorders are at higher risk for TBIs. Research suggests that 29–58% of patients admitted to hospitals with a TBI have alcohol in their systems at the time of admission (Miller & Werner, 2011). As a result of the disruption of protective mechanisms such as the blood-brain barrier, active alcohol use can enhance TBI neural damage suffered by the individual (Miller & Werner, 2011). Unsworth and Mathias (2016) determined by meta-analysis that a history of misusing alcohol or drugs does have poorer neurological outcomes, but further research is needed in this area to understand the impact of prior SUD on TBI.

The effects of a TBI vary from one individual to the next, depending on (a) the cause of the brain injury, (b) the location of the injury, (c) the extent of the injury, and (d) the individual's level of function before the injury. A patient with a mild concussion suffered while playing football will usually have different presenting symptoms than a patient who suffered a major TBI in a motor vehicle accident, for example. In addition, the degree of recovery will vary from one patient to the next, although the greater the damage to the brain the less likely it is that the individual will return to his or her pre-injury level of function. A formerly high-functioning student might, after suffering a serious TBI, struggle to perform simple mathematics problems or even to sign his or her name. This hypothetical student, whose life once held such promise, might now require lifelong psychosocial support. There are also often post-injury changes in personality that might push pre-injury relationships beyond the breaking point. This hypothetical student might refuse to acknowledge the role that chemicals played in the injury

²⁶ A trend that, unfortunately, appears quite prevalent in most large organizations.

²⁷ The subject of TBIs is worthy of a large book in its own right. The reader is referred to any of a large number of neurology or neuropsychology textbooks.

(if they did), and might conceivably not understand that he or she has suffered a TBI.

Denial is a difficult problem for persons who work with individuals who have suffered a TBI. Pre-injury or post-injury cognitive deficits might not allow the individual to understand the relationship between these two disorders. The individual might have developed **retrograde amnesia**²⁸ as a result of the TBI: The person might not remember consuming alcohol or illicit drugs before their injury. Some individuals might be reluctant to give up recreational chemicals, which they have come to accept as a way to adjust to their new lives. If they should continue to misuse chemicals, they might discover that they have developed a medication (or chemical) sensitivity, experiencing stronger reactions to these chemicals than a person of the same age who had not experienced a TBI. Their apparent denial might, however, alternatively, be a reflection of the therapeutic relationship and their lack of trust in the therapist.

The self-medication hypothesis would appear at face value to have some validity with this subpopulation: It has been suggested that patients with TBIs might turn to alcohol or drugs as a way to self-medicate their frustration. Persons who have suffered a traumatic brain injury might with justification feel that they are “different” from others. Alcohol and/or illicit drug misuse offers them one avenue through which they can associate with others. An unfortunate social attitude is that the person with a TBI is entitled to misuse alcohol or illicit drugs because of what he or she has endured as a result of his or her TBI. Substance rehabilitation professionals who work with individuals with co-occurring SUDs and TBIs should be well versed in each condition. For example, medical staff must often differentiate between legitimate medication requests by the individual to treat medical or psychiatric conditions, and drug-seeking by that person. A concurrent treatment approach, adjusted to the individual’s level of function and possible altered mental abilities, is the best treatment approach.

Post-Concussion Syndrome (PCS)

Persons who have suffered a concussion represent a subgroup of traumatic brain injury cases. For years, physicians had been taught that the individual who had suffered a mild concussion returned to their baseline level of function within a few minutes or at most hours. In the last 15 years it has been discovered that the effects of even a mild concussion persist longer than this. Persons who had suffered a mild concussion often developed mild cognitive problems,

fatigue, dizziness, headaches, and personality changes, which generally resolve in the first weeks or months after the person suffered the concussion. In some cases, the post-injury changes might last a year or longer. The prognosis is worse if the person has suffered a loss of consciousness at the time of the injury. Often, especially in cases of mild post-concussion syndrome, the post-injury cognitive deficits are detectable only on neuropsychological testing. However, as the severity of the TBI resulting in a concussion increases, the possibility of more severe cognitive damage and personality change increases.

PCS is influenced by a range of factors, some of which are generic to all cases of TBI. Other factors include (but are not limited to) the individual’s pre-injury personality, secondary gain from the injury (being excused from work or school assignments, or attempts to avoid pending legal charges, for example), and any litigation pending as a result of the injury. All cases of known or suspected PCS should be referred to a neuropsychologist or neurologist for assessment and treatment recommendations, and substance rehabilitation professionals who work with persons with PCS should be trained in this specialty before attempting to work with these individuals.

Clients with Co-Occurring Diagnoses and Medication Compliance

As will be discussed in Chapter 33, medication compliance is a problem for all medical patients. This topic is discussed separately in this chapter because of the special nature of persons with co-occurring disorders. As a group, clients with co-occurring disorders are 8.1 times more likely to be non-compliant with their medication(s) than traditional psychiatric clients (Drake, 2007; RachBeisel, Scott, & Dixon, 1999). This complicates the treatment of both their psychiatric and substance use disorders. Medication noncompliance might be expressed in a variety of ways, such as (a) refusing to take prescribed medications, (b) continuing to use alcohol and/or illicit drugs, or (c) selectively taking only those medications that will provide the desired effects.²⁹ To avoid potentially dangerous interactions, some clients with co-occurring disorders will discontinue psychiatric medications in anticipation of recreational drug use. The most common reason for these behaviors is not to self-medicate psychiatric distress, or to avoid unpleasant side effects, but simply to enjoy the “high” experienced through recreational chemical use.

²⁸See Glossary.

²⁹ Another issue, discussed in Chapter 33, is inability to afford prescribed medications. Since this does not reflect willful noncompliance, it will not be discussed further in this chapter.

It was noted in the last paragraph that sometimes clients with co-occurring disorders will selectively refuse certain medications: Many psychiatric medications have a significant misuse potential of their own. For example, occasionally an individual will hoard anticholinergic capsules or pills³⁰ and then ingest them all at once for their psychoactive effects (Buhrich, Weller, & Kevans, 2000). These medications may also potentiate the effects of the amphetamine compound and might be misused for this reason. Clients with co-occurring disorders may misuse psychiatric medications when they are unable to access more desired drugs of misuse. Urine toxicology testing³¹ is useful in the identification of persons who fail to have prescribed medications in their urine, or who have metabolites of recreational drugs in their urine.

Treatment Approaches with Clients with Co-Occurring Disorders

Patients with co-occurring disorders have long been shunned by both the psychiatric and substance rehabilitation communities. Now treatment approaches are starting to emerge to guide professionals in their work with these clients. However, it should be noted that many of these treatment approaches rest not on a foundation of clinical research, but on expert opinion (Watkins et al., 2001) and anecdotal case studies. There is a “dearth of empirically sound interventions” for clients with co-occurring disorders (Bellack, Bennett, Gearon, Brown, & Yang, 2006, p. 427). Given the prevalence of co-occurring disorders already presented in this chapter, it is certainly important to realize that less than 8% of those struggling with an SUD and another mental health diagnosis receive treatment for both, and over half receive treatment for neither (SAMHSA, 2016).

It is believed that the ideal treatment setting for clients with co-occurring diagnoses is an **integrated treatment program**, in which both the SUD and the individual’s psychiatric problems might be addressed simultaneously by treatment professionals from various fields of training, who work as a team to help the patient (Busch et al., 2005; Pankiewicz, 2008; Priester et al., 2016). Such treatment programs achieve long-term abstinence rates of about 15%, which approximates the abstinence rate achieved in normal clients who enter rehabilitation (Pankiewicz, 2008). Others indicate that the integrated treatment that is most effective would be when the same staff are able to treat both co-occurring disorders (Sadock et al., 2015).

More commonly, clients with co-occurring disorders are referred to treatment facilities that use the **serial treatment approach** (Goldsmith & Garlapati, 2004). In such a program, the most serious issue is addressed until that condition is stabilized, and then the client is transferred to a different unit so that the other disorder might be addressed. This might be either a different unit within the same facility, or at a different rehabilitation facility entirely. A serious weakness of this treatment approach is that clients rarely follow through and enter the second program (Busch et al., 2005; Mueser et al., 2003). Even if sequential admissions are accomplished, treatment stays allowed under the managed care programs are often inadequate for treatment of either condition. Pankiewicz, (2008) estimated that only 5% of patients with co-occurring disorders are treated in such a series of programs will achieve long-term abstinence.

An alternative to the serial treatment model is the **parallel treatment model**, in which both conditions are addressed simultaneously, but in different sections of the same facility, without a team approach (Busch et al., 2005). Hypothetically, the client’s SUD might be addressed on the second floor of the east wing of a hospital setting, while the psychiatric illness is addressed on the fourth floor of the west wing of the same facility. There are numerous drawbacks to this approach, including poor communications between treatment staff on the different units, and the act of physically moving the patient from one floor to another (where she or he must adjust to the treatment setting again) at a time of special vulnerability. Yet another drawback is that this model interferes with the development of a firm therapeutic relationship between the therapist on one unit and the patient, who upon stabilization will be transferred to another unit (Drake & Mueser, 2002). Obviously, this makes for an inefficient treatment process, and this model is the least effective of the three models discussed thus far (Drake, Mueser, Brunette, & McHugo, 2004; Ross, 2008).

The Stages of Treatment

Substance rehabilitation for clients with co-occurring disorders is more complicated than for clients with an SUD but without a concurrent mental illness. The first goal in working with the client with co-occurring disorders is the establishment of a good therapeutic relationship (Drake & Mueser, 2002). This task might take a protracted period of time, and the therapist must make every effort to be nonconfrontational, optimistic, and empathetic, avoid making moralistic judgments, and work on establishing a therapeutic relationship (Patrick, 2003).

The second phase of treatment is *persuasion* (Drake & Mueser, 2002), *engagement*, or *motivational enhancement/engagement* (Geppert & Minkoff, 2004). During this phase

³⁰ Often prescribed to help control the unpleasant side effects of psychotropic medications being used to treat the mental illness.

³¹ Discussed in Chapter 33.

of rehabilitation, the staff works to help the client understand the relationship between her or his substance use disorder and psychiatric problems. Issues such as medication noncompliance and its relationship to decompensation and rehospitalization are addressed during this phase. Breaking through the client's denial without causing increased psychiatric distress is also carried out during this phase, so that the client might see that abstinence is worthwhile both in reduced hospitalization, and because substance misuse is destructive in its own right (Geppert & Minkoff, 2004; Patrick, 2003).

The third phase of rehabilitation is *active treatment*, during which time the staff teach the client coping skills, help her or him find sources of support, and manage his or her illness (Drake & Mueser, 2002). This stage has also been called that of *prolonged stabilization: active treatment/relapse prevention* (Geppert & Minkoff, 2004). The client is at high risk for relapse during this stage, if only because the motivation inherent in a psychiatric emergency has eased (Drake, 2007). The use of group therapy is often of value during this phase, although because of the perceived stigma associated with mental illness in the eyes of the clients, it is best that these therapy groups be held on the psychiatric ward of the treatment facility.

One of the advantages of therapy groups is that more experienced patients might share their experience(s) of how even limited alcohol or drug misuse contributed to their psychiatric decompensation, and the problems in living that they encountered the last time they had finished rehabilitation and returned to independent living. Such groups may reduce rehospitalization rates, although research has demonstrated that clients with co-occurring disorders tend to continue to misuse chemicals after discharge from treatment. During the third phase of treatment, relapse prevention becomes a major focus. The patient and treatment staff identify relapse triggers that contribute not only to renewed substance use, but also to psychiatric decompensation. Another focus is on helping the client learn how to build a substance-free support system, as failure to establish such a substance-free support system is a major factor contributing to relapse for this population (Swartz et al., 2006).

It should be pointed out that, while many of the techniques developed for use with the average client misusing substances will work with clients with co-occurring disorders, there is no single treatment method or intervention that is equally effective with each individual client (Geppert & Minkoff, 2004). Thus, treatment methods and interventions should be individualized, taking into account where the patient is in the recovery process, her or his psychiatric status, and her or his willingness to change (Geppert & Minkoff, 2004). It should be noted that confrontational techniques often used with clients misusing substances are rarely effective with clients with co-occurring disorders, and may even

be counterproductive (Ross, 2008). When confrontation is needed, it should be less intense than with more traditional substance-misusing patients.

Once the individual's psychiatric problems have been brought under control, his or her substance-related defenses again begin to operate, and the client will then return to the position of protecting the substance use. Clients with co-occurring disorders often believe that once their psychiatric problems are controlled they are no longer in danger of becoming addicted to the chemical(s) being used. The client might try to tell the counselor what s/he wants to hear, rather than what they need to say to address his or her substance use disorder, or to avoid confrontation that is viewed as being harsh, rejecting, and confrontational by the client. This is why group therapy is so useful during this phase of treatment: Patients are often more willing to listen to another patient who shares her or his experiences with substance use following an earlier hospitalization than they are to a counselor. Also, group members are able to problem-solve together, with one patient sharing his or her wisdom with another as they discuss life's problems.

The Outcome of Treatment

One variable that has been found to affect treatment outcome was the home environment into which the patient was discharged (Stahler, Mennis, Cotlar, & Baron, 2009). Discharging a patient into the environment where they misused chemicals will activate location-triggered substance use cues, and the effects of this are compounded if the patient lives a great distance from 12-step support groups (Stahler et al., 2009). This topic has opened a new avenue for clinical research that might offer insights into improving treatment outcomes.

While complete abstinence is the desired goal, the program staff must also accept that for most clients with co-occurring disorders, a major reduction in substance use levels might be a more realistic outcome, at least at first. This "harm-reduction" approach will limit the amount of damage to the individual and his or her life until she or he can realize the need for abstinence. Progress is often slow, with frequent regressions to an earlier level of functioning. With continued patience, it is often possible for clients with co-occurring disorders to discontinue recreational drug and alcohol use over time. But this is the end point of a long, difficult process for both the client and treatment staff.

Ancillary Issue: Smoking

Statistically, individuals who smoke cigarettes and also have mental illness are more likely to die from smoking-related illness than from any other cause (Kalman, 2010).

Unfortunately, the already dismal smoking cessation rate for smokers is even worse for those with a major mental illness. Not only are those with some form of mental illness twice as likely to smoke, but the trend is heading toward those with mental illness making up the majority of the smokers in the United States in the near future (Atkins, 2014).

Chapter Summary

The client with co-occurring disorders presents a difficult challenge for health care professionals. Once thought to make up only a small fraction of psychiatric patients, it is now accepted that clients with co-occurring disorders are perhaps a majority of those seen in a psychiatric setting. However, diagnosis of concurrent psychiatric and substance problems is complicated by the fact that virtually every symptom of mental illness can be simulated by active substance use or the

various withdrawal syndromes. Taking a careful clinical history is key to identifying those patients who have a preexisting mental illness, as opposed to those whose psychiatric symptoms are induced by the substance use or withdrawal.

Clinical evidence suggests that clients with co-occurring disorders often use the problems induced by one disorder to protect the other, a process called **free-floating denial**. If the health care professional attempts to focus on the client's health or psychiatric problems, she or he will shift the focus on to her or his SUD. If the substance rehabilitation professional attempts to focus on the client's SUD, the client will try to discuss health issues instead, thus blocking therapeutic inquiry into areas that might induce change. However, it is possible to work with clients with co-occurring disorders if the professional is willing to endure extended periods of minimal progress on the part of the client, if not outright regression. But over time, it is possible to assist many clients with co-occurring disorders to commit to recovery.



CHAPTER 26

The Biopsychosocial Model of the Addictions

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 26.1** Understand the various models of addiction
 - 26.2** Describe the biopsychosocial model and the separate components of this model
 - 26.3** Review the typical applications for the separate components of the biopsychosocial model
 - 26.4** Describe the reactions against the separate components of the model
 - 26.5** Consider the reactions to the biopsychosocial model as a whole
-

Treat the person with the disease, not the disease in the person.

—Sir William Osler (1910)

Introduction

For many years, the medical sciences have adhered to the biomedical model of disease, which is an outgrowth of the discovery in the late 19th century that many common disorders were the result of bacterial or viral infections (Johnson, 2012a). While the biomedical model was instrumental in increasing life expectancy in the United States from 43 years in 1900 to approximately 77 years for an infant born in 2000, it failed to recognize the psychosocial components of illness. Arguably, this could be a reflection of the mind-body dualism that has dominated research in the behavioral sciences and medicine for so many centuries (Shadel & Scharf, 2012).

Recently it has been acknowledged that “unbiased” research is difficult to achieve. Great care must be used to ensure that the results of a research study have not been distorted by the perspective of the *viewer* rather than the nature of the disorder under investigation. Even unconscious bias might influence the design of a research study so that the results meet the researcher’s expectations, for example. Arguably, this is an unintended side effect of the biomedical model of medicine and its narrow focus on treating what it defines as *medical* disorders: Health care professionals viewed the substance use disorders (SUDs) as a medical problem, mental health professionals viewed them as a mental health issue, and substance rehabilitation professionals viewed them as a problem best addressed by themselves.

In reality, these territorial disputes serve to obscure the fact that categories of “biological” factors or “psychosocial” factors were artificial constructs used to help explain the complex phenomenon of human behavior. These constructs were not intended to be mutually exclusive: Our narrow perspective on the substance use disorders made it appear that way. The individual’s substance use reflects a combination of person-specific biological, psychological, and social influences (Winters et al., 2012). The substance use disorders are a *common end point* reached by different routes. In this chapter, the bio/psycho/social disorder of the SUDs will be reviewed.

I. Biology: The “Bio” Part of the Bio/Psycho/Social Model

Definition

The biological component of the bio/psycho/social model is the “anatomical, structural and molecular substrates of a disease” such as the substance use disorders, and the effects of that disorder on the biological functioning of the individual (Sadock, Sadock, & Ruiz, 2015, p. 3).

History

Proponents of the medical, or “disease,” model often point out that Dr. Benjamin Rush first suggested that alcoholism was a disease more than 260 years ago. When he made this observation, a “disease” was classified as something that caused an imbalance in the nervous system (Meyer, 1996). By this standard, substance use disorders (SUDs) would appear to meet the definition of a “disease” state, although one that is quite different from what Dr. Rush envisioned. The substance use disorders are now thought to be the result of a biological dysfunction, possibly on the cellular or even the molecular level, which alters normal biological processes within the body such as the reward system. However, the biological model of addictions has been challenged in spite of its contributions to the understanding of the SUDs (Volkow, Koob, & McLellan, 2016).

Process

Nature has provided us with a reward system designed to reinforce behaviors that are of benefit to the individual or the species: eating when we are hungry, drinking water when we are thirsty, or taking advantage of opportunities for sex when possible. These are the clearest examples of the role that the

reward system provides; however, it is also involved in the feeling of warmth and joy that we feel when reuniting with a loved one after a short absence, as well as the pair-bonding process that occurs when a mother and infant gaze into each other’s eyes. In all these situations, the reward system of the brain is activated, impressing upon the individual the message that what he or she just did is important and should be repeated when appropriate.

Unfortunately, we do not live only in the “natural” world: We are exposed to various chemicals of human making that now have the potential to overwhelm our natural neurotransmitter system. By accident, certain compounds developed by chemists are capable of creating an intense but false signal in the brain’s reward system, memory centers, and the higher cortical areas that control reward-seeking behavior(s). Collectively, activation of these regions of the brain gives the false signal that what the individual just did (in this case, using a substance of misuse) is really, *really* important. This is the neurological basis of the *pharmacological reward potential* of that compound. Strong substance-use memories are formed, helping to shape behavioral decisions that hopefully will lead to further drug-induced rewards (D. Brown, 2006; Bruijnzeel, Repetto, & Gold, 2004; Conrod & Nikolaou, 2016; Gendel, 2006; Lewis, 2011). Essentially, a normal biological process that evolved to help early humans survive has been subverted by the reward potential of compounds that humankind has invented (Marcus, 2008).

Support for the biological model of the addictions is found in research suggesting that under certain conditions the release of the neurotransmitter dopamine in select regions of the brain initiates a *neurotransmitter cascade* in the reward system that is subjectively experienced as a sense of pleasure. This neurotransmitter cascade also reinforces the effects of Δ FosB,¹ especially in the nucleus accumbens region of the brain, where Δ FosB is involved in the process of learning on a neural level. In the natural world, it is to the individual’s advantage to recall cues that identify natural rewards such as food, water, or sex, memories that are aided by the action of Δ FosB in the nucleus accumbens. This system is perfectly designed to assist the individual to survive in a harsh prehistoric environment where survival was problematic at best and life exceptionally short by our standards. This system continued to flawlessly serve our needs until the late 19th and 20th centuries, when compound after compound that had greater misuse potential was isolated or developed. Suddenly society was faced with the widespread misuse of chemicals, and scientists have struggled to develop a paradigm that would allow them to understand the etiology of

¹See Glossary

this phenomenon and provide a framework within which to treat it. In the next sections, we will discuss some of the more influential models that help to shape our understanding and treatment of the SUDs.

Biological Determinism

At its extreme, humans are viewed as biological robots whose behavior is predetermined at the beginning of time (Ferris, 2012). From such a perspective, it could be argued that with sufficient knowledge of the interactions of the atoms within the individual's body it would be possible to predict that individual's current and future behavior. From this perspective, *free will is only an illusion* unworthy of study, since the individual's actions are predetermined by the nature of the universe (Siegel, 2013), or that free will is only a social construct (Gazzaniga, 2015b). This places biological determinist theorists in the position of affirming that our behavior is biologically predetermined *as long as you ignore certain convenient truths*. For example, were the actions of the individual who challenges biological determinism preordained or do these thoughts reflect personal choice? Echoes of this fundamental conflict are often heard in the courts: If an individual who committed a murder is found to have a biochemical imbalance or perhaps a brain tumor, are they responsible for their decisions and actions? Gutmann (2015) argues that while neurosciences might reveal a great deal of the biological foundation for decision making, such discoveries should not negate personal responsibility.

At the risk of providing a gross oversimplification, the “individual” is usually viewed by moderate biological determinists as being the result of their biological heritage, their current internal environment, and their past and current interactions with the external environment. Hunger is a very good example: If you are hungry, you go look for something to eat. From this perspective, the substance use disorders reflect an unidentified biological predisposition over which the individual has no control, just as the individual cited in the earlier example has no control over his or her sense of being hungry. They are viewed as being powerless over their substance use disorder by those who adhere to the biological determinist perspective on human behavior.

Jellinek's Work²

Archaeologists now believe that by the time modern humans emerged, they knew which fruits and tubers would ferment at certain times of the year to provide a naturally occurring

cocktail or two (Tucker, 2011). It is unlikely that alcohol use was problematic during this era since it was so difficult to obtain in even limited quantities. By the late 19th century, however, alcohol misuse/addiction was a recognized problem for society. Individuals who had an alcohol use disorder (AUD) were viewed as being morally weak, a perspective that will be discussed later in this chapter. In contrast to this belief, the physician E. M. Jellinek (1952, 1960) argued that alcoholism was a disease just like cancer or pneumonia, rather than a moral weakness. He reasoned that, like other disease states, alcoholism presented a specific pattern of symptoms, which in the case of alcohol dependence included (a) a loss of control over one's drinking, (b) a progression of physical and psychosocial problems, and (c) if left untreated, could cause the individual's death. Further, Jellinek (1952) argued that the addiction to alcohol progressed through four different stages:

1. The **pre-alcoholic** stage, marked by individual's use of alcohol to self-medicate social tension, frustration, and anxiety. The individual is no longer drinking on a purely social basis, but has started to engage in what is called “relief drinking.”
2. If the individual continues to engage in “relief” drinking, s/he slips closer to, and eventually enters the **prodromal stage** of alcohol use. During this phase, the individual begins to demonstrate such alcohol-related problems as “blackouts,” guilt over one's behavior while intoxicated, and the urge to hide one's drinking from others.
3. With the continued use of alcohol, the individual eventually becomes physically dependent on alcohol. The individual's self-esteem suffers from his/her alcohol use, and social activities that do not involve the use of alcohol are shunned in favor of alcohol-centered activities. At times, the individual will make an effort to reassert control over alcohol, only to return to abusive drinking again after a period of time.
4. Finally, with continued alcohol use, the individual would enter the **chronic stage** of alcohol use. During this phase, the individual will demonstrate symptoms such as a deterioration in morals, the use of alcohol substitutes when ethyl alcohol is not available,³ the development of psychomotor “tremors” after drinking, and possibly drinking with one's social inferiors.

Jellinek's (1960) model was strongly biased in the direction of biological determinism, as evidenced by his belief that once an alcohol use disorder developed, it was automatically progressive. In his revision of his earlier work, Jellinek (1960) suggested that there were different patterns of alcohol dependence rather than a single pattern of drinking.

²It is important to note that Jellinek's work only addressed the addiction to alcohol, though it *has* been applied to other forms of chemical dependency as well as some of the behavioral addictions by some clinicians.

³Discussed in Chapter 5.

This paradigm did offer physicians an alternative to the moral model that had been the generally accepted view of the alcohol use disorders for generations. Jellinek's theory provided a framework within which physicians could (1) classify different patterns of alcohol misuse as opposed to the more restrictive dichotomous view that the person was either an alcoholic or not, (2) make the alcohol use disorders (AUDs) worthy of study by science, and (3) allow the individual access to medical care. Finally, (4) the Jellinek model attributed the individual's AUD not to a lack of willpower, but to a physical disease state over which the individual had no control (Fletcher, 2013). The Jellinek model is not without its critics, however, and these challenges to the model will be discussed later in this chapter.

The Genetic Inheritance Theories

The genetic inheritance theories are strongly deterministic (according to this perspective, you *are* only your genetic heritage), although many variations of the genetic inheritance theories accept that the environment also helps to shape behavior. For example, in his discussion of the evolution of *Homo sapiens*, Ian Tattersall (2012) expressed a strong deterministic genetic inheritance stance as evidenced by the following quote:

Individual human beings are substantially—though not entirely—the products of their own particular genomes, coming into the world as broadly the kind of persons they will be as adults.

Tattersall (2012, p. 229)⁴

From this perspective, the environment and life experiences have the potential to facilitate or inhibit the expression of the individual's biological inheritance. To the moderate biological determinist, it is the individual's biological heritage that is the most powerful determinant of their behavior, with environmental and life influences playing a secondary role in shaping the individual's behavior.

The team of Cloninger, Bohman, and Sigvardsson (1981, 1996) appears to have adopted such a modified determinist view on the basis of their research. For their first study, the authors drew on the extensive records of 3,000 boys adopted shortly after birth. In some cases, one of the child's birth parents had indications of an alcohol use disorder (AUD), and at least one adoptive parent showed indications of an AUD. Other children whose parent(s) had

indicators of an AUD were adopted shortly after birth by parents who did not have an alcohol use disorder. A third subgroup were adoptees whose birth parents did not have indicators of an alcohol use disorder but who were raised in families where at least one parent had indications of an AUD. The second study was a replication study, which involved both male and female adoptees. The results of these studies rocked the world of psychiatry.

The authors found that the possibility of an individual developing an alcohol use disorder varied between subgroups, and that there were differences in the *pattern* of drinking between members of these various groups. Group one was comprised of individuals who engaged in the moderate use of alcohol in young adulthood, demonstrated minimal involvement in antisocial behaviors, were frequently depressed, sought social approval, avoided high-risk or novel situations, and typically developed an alcohol use disorder in later adulthood (Hesselbrock & Hesselbrock, 2007). These individuals were classified as "*Type I*" (also known as "*Late-Onset*" or "*Type 'A'*") drinkers.

The second group consisted of individuals who were risk-takers, who tended to seek out novelty, engaged in violent behaviors, consumed alcohol for pleasure, and frequently demonstrated alcohol use disorders before the age of 25 years (Hesselbrock & Hesselbrock, 2007). These individuals were classified as "*Type II*" (or "*Early-Onset*" or "*Type 'B'*"), alcohol-dependent. Statistically, the heritability for Type II alcoholism was somewhat higher than for Type I alcoholism, suggesting at least some degree of genetic vulnerability that was transmitted from natural father to the son, although both are considered heritable, yet distinct forms (Sigvardsson, Bohman, & Cloninger, 1996). A similar study completed by Kendler and colleagues (2012) suggested that this pattern was also true for women adopted at birth. Again, the authors drew upon the extensive adoption records maintained in Scandinavia and concluded that drug misuse was significantly higher for adopted offspring of birth parents with an AUD. The authors also noted that various nonspecific social and environmental factors influenced the expression of the suspected genetic predisposition for the development of a substance use disorder. These environmental factors are thought to work at least in part through the process known as epigenetics.

Epigenetics⁵

As scientists learned more about the human genome, they began to find that the interaction between the individual's

⁴Admittedly, the topic of Tattersall's (2012) rather interesting book was the evolution of the species. However, the author of this text submits that his observation about the effects of the individual's genome on their growth is still relevant to the topic of this text.

⁵The subject of epigenetics is an emerging field of study that is far too complicated to be discussed in detail in this text.

genetic heritage and their environment is much more complicated than originally thought. One process through which environmental forces can alter the expression of the individual's genes is what is known as **epigenetics**. This new field of study offers the potential for insights into not only the substance use disorders but also a wide range of other neurobehavioral and neurological disorders⁶ (Starkman, Sakharkar, & Pandey, 2012). Essentially epigenetics refers to:

stable, but potentially reversible, alterations in a cell's genetic information that results in changes in gene expression but do not involve changes in the underlying DNA sequence (i.e. mutations).

Kobor and Weinberg (2011, p. 300, italics added)

It has been known since the 1950s that DNA molecules form a double helix within the cell nucleus. However, since most DNA exists only within the nucleus of the cell, it is necessary for a mechanism to take the genetic information contained in the DNA through the nucleus wall into the intracellular environment to control the function of the cell. This substance is known as **messenger RNA**⁷ (mRNA), which encodes that portion of the DNA chain necessary to instruct the cell to carry out a desired function such as the production of different proteins within the cell. According to the theory of epigenetics, molecules known as *histones* attach to the DNA double helix at what are known as promoter regions, much as the rungs of a ladder are attached to the sides of the ladder at specific points (Nasrallah, 2011). There are five known families of histones (Pluess, 2015). These histones are involved in gene expression through their interactions with DNA, which include at least seven types of modification, of which two are most understood at this point: (a) *methylation* (*mono-*, *di-*, or *tri-*), which may block expression of a gene, or in some cases increase the expression of a gene, and (b) *acetylation*, which usually is involved in the expression of a gene) (Griffiths & Unwin, 2016; Pluess, 2015). To continue with the analogy of a ladder, if a rung of the ladder were to be removed, it would be difficult if not impossible for a person to climb the ladder beyond that point. In a similar manner, the methylation histone molecules may attach to the double helix of the DNA, blocking the expression of a gene without altering the gene itself (Hurley, 2013; Nasrallah, 2011; Starkman et al., 2012).

Initially it was thought that epigenetic changes took place only during the prenatal phase of life (Hurley, 2013).

Currently it is thought that there are *critical periods* in life when epigenetic changes are more likely to take place, including the prenatal period, childhood, puberty, and possibly young adulthood, although it is also quite likely that changes can occur throughout life (Pluess, 2015). These are time periods when it is thought that alcohol, tobacco, and illicit drugs influence the development of methylation histones, which in turn attach to the DNA double helix, blocking the full expression of genes (Starkman et al., 2012; Yi Wong, Mill, & Fernandes, 2010). The messenger RNA is then able to copy only that portion of the DNA molecule not blocked by an inhibitory histone, limiting the instructions that it can transmit from the DNA to the cell outside of the nucleus. The process of epigenetics helps to explain how environmental forces can alter the expression of certain genes, and future research will continue to give us a greater understanding of how genetics and experiences interact (Turner, 2016).

For reasons that are still unknown, the influence of environmentally altered genetic expression does not appear to be limited to one generation. To some degree, altered genetic expression can be passed from one generation to the next (Hurley, 2013). For example, Nasrallah (2011) found that men who smoked before puberty ultimately had children with heavier body weights than did men who did not smoke. Further, the author noted, animals subjected to caloric restriction live about 30% longer than do those that receive normal diets, and their offspring live 20% longer on average even if they were not subjected to caloric restriction. Research is also pointing toward the impact on offspring of cannabis use, even prior to conception (Szutorisz & Hurd, 2016), with additional research continuing to confirm that epigenetics can create an impact across generations (Vassoler & Sadri-Vakili, 2016). Thus, epigenetic changes hold the potential to influence not only the individual but also the individual's offspring.

Epigenetic changes to cellular DNA are not always negative but might also contribute to the development of resiliency (Hurley, 2013). While the process of epigenetics is still being explored, it holds the potential to aid in the development of pharmaceuticals that will enhance resilience and erase negative epigenetic changes.

Neurobehavioral Theories

Another biological theory, one that overlaps with biological determinism, is the neurobehavioral school of thought. Proponents of these theories maintain that through interactions between the environment and the individual, neurological pathways are established, and with repeated activation are reinforced. Neurons that fire together reinforce the neurochemical bonds between those neurons so that they might work as a functional unit more easily when next called

⁶Which might explain why, if one member of a pair of identical twins has an alcohol use disorder, the probability that the other twin will develop an alcohol use disorder is approximately 50-50, for example.

⁷See Glossary.

upon. Alcohol use cues reportedly activate the ventral striatum in the brain as well as regions involved in decision making and emotional and cognitive control systems (Naqvi & Morgenstern, 2015). One behavioral outcome of the activation of these regions of the brain is that the individual is predisposed to engage in short-term behaviors with a high probability of obtaining a reward than in long-term activities with an uncertain possibility of being rewarded, especially if those regions of the brain involved in decision making and emotional and cognitive control are not fully functional (Naqvi & Morgenstern, 2015). According to this theory, drugs can alter the normal neurochemical balance within the central nervous system, especially those involved in the reward system. This alteration may be far more impactful than natural neurotransmitters, increasing the probability that the individual will wish to re-experience that reward experience.

With repeated activation of the reward cascade, the process of *over-learning*⁸ is initiated, in this case resulting in the reliance on one or more chemicals to achieve the desired state of mind again. Cigarette smoking provides an excellent example of this process: Each time the smoker inhales, he or she reinforces the neural connections between smoking and pleasure, stress relief, etc. This process might be repeated hundreds of times each day, allow for the over-learning of this process. The individual also becomes very sensitive to environmental cues associated with substance-induced pleasure (“Addiction and the problem of relapse,” 2007; Viamontes & Beitman, 2006) or internal sensations associated with the danger of experiencing substance withdrawal (van der Kolk, 2014). This learning process appears to involve the regions of the brain known as the **amygdala**⁹ and **hippocampus**,¹⁰ regions of the brain involved with memory formation. Under normal circumstances, the individual needs to know when not to engage in a specific behavior (such as going to obtain water from a nearby river if a predator is in the area). Behavior is shaped by a delicate balance of activation and inhibition neural systems, both of which are influenced by memories in the brain. This process plays a role in the survival of the person and contributes to the ongoing process of learning. However, drugs can trigger a reward cascade that is far more intense than that generated by normal reinforcers, and it can cause those regions of the brain associated with behavioral inhibition to become less active, paving the way for repeated misuse of the chemical(s) (Bechara, 2006; Gendel, 2006; Volkow, 2006a).

⁸Again, this illustrates the interconnectedness of the bio/psycho/social model since learning is both a biological process and a psychological process.

⁹See Glossary.

¹⁰See Glossary.

THE BIOLOGICAL DIFFERENCES THEORIES

The biological differences theories overlap the neurobehavioral schools of thought. Researchers tried to identify and isolate a biological difference between those individuals who were alcohol-dependent and those who were not. These theories are moderately deterministic in nature and also overlap with the neurobehavioral theories discussed in the last section. The biological differences theories hold that there are differences, either in the brain or in how the body metabolizes the drugs, that increase the potential for a substance use disorder developing in certain individuals. There is some evidence to support these theories: Research has shown that after 1–2 weeks of habitual daily drinking there is a short-term 30% increase in the speed of alcohol biotransformation, allowing the drinker to consume more alcohol before reaching their desired state of intoxication (Schuckit, 2017). Individuals whose genetic makeup allows them to produce more of the enzymes alcohol dehydrogenase and aldehyde dehydrogenase would in theory be able to biotransform alcohol more rapidly, encouraging the excessive use of alcohol to reach and maintain a desired state of intoxication (Foroud & Phillips, 2012). However, these findings are preliminary, and there is a need for further research into this area.

Another example of the biological differences between individuals who use substances and those who do not was identified by Nurnberger and Bierut (2007). The authors found that individuals who were connected to electrodes that measured brain wave activity and then exposed to a standard stimulus (a strobe light) exhibited a short spike in electrical activity in the brain between 300 and 500 milliseconds after the stimulus began.¹¹ As a group, it was found that individuals with an AUD, as well as their children, had a weaker response to this stimulus than did nondrinkers. Other lines of research suggest that individuals who have been identified as being high risk-takers appear to have different levels of the enzyme monoamine oxidase, suggesting that some behaviors reflect biological predisposition to some degree (Zuckerman & Kuhlman, 2000). Newer research continues to explore what genetic and environmental influences can be separated to explain high risk-taking behaviors, with findings indicating that additive effects of genes may be contributing rather than specific dominant genes (Wang, Zheng, Xuan, Chen, & Li, 2016).

The discovery that the number of neurons in the brain is not static but is influenced by the processes of neural pruning and **neurogenesis**¹² suggests another avenue through which such biological differences might be expressed. It was

¹¹Technically, this is called the P-300 response.

¹²See Glossary.

discovered by Noonan, Bulin, Fuller, and Eisch (2010) that cocaine appears to suppress the process of neurogenesis in the hippocampal region of the brain of adult rats, reducing the growth of new neurons in the hippocampus. This region of the brain is involved in memory formation. The authors postulated that this might be a mechanism through which drug craving is generated in individuals who formerly used cocaine in the early stages of recovery.¹³ This study provides evidence that cocaine use does alter the pattern of neural growth in the brains of the rats in the study. Unfortunately, it is not known whether these changes are permanent or, like the epigenetic process itself, can reverse itself in time. Further research on cocaine as well as other drugs continues to explore this topic, and future research with humans will help to clarify whether neurogenesis can be stimulated in some way so as to reverse the dysfunction (Castilla-Ortega et al., 2016).

Marc Schuckit's (1994) study is often cited as evidence of biological vulnerability to alcohol use disorders. Forty percent of those men who were raised by a father identified as having an alcohol use disorder, but only 10% of the control group, demonstrated a greater sensitivity to a standard dose of alcohol. A decade later, the author went back and found that 56% of the men who had an abnormally low response to alcohol had developed an alcohol use disorder. This was called the *low level response theory* and was interpreted as evidence that a low physical response to a standard dose of alcohol might serve as a biological marker for the later development of an alcohol use disorder.

Research support for the low level response theory has been mixed (King, de Wit, McNamara, & Cao, 2011). For a subgroup of drinkers, alcohol appears to have a stimulant effect while blood alcohol levels are still rising, a characteristic that King and colleagues (2011) found to be predictive of future binge drinking. The frequency of binge drinking was in turn found to be predictive of future alcohol use problems, according to the authors. The authors speculated that low level responses observed by Schuckit (1994) might have reflected individuals' response to alcohol when their blood alcohol levels were dropping and not while they were increasing, confounding the study's outcome (King et al., 2011). Ongoing research continues, with research considering multiple factors of impact on response to alcohol, including differing levels of cortisol in stress reactions (Brkic, Söderpalm, & Gordh, 2016).

THE DOPAMINE D₂ HYPOTHESIS

The *dopamine D₂ hypothesis* overlaps with the biological differences school of thought outlined in the last section. There

are at least five known subtypes of dopamine receptors in the human brain (Ivanov, Scholz, Palmero, & Newcorn, 2006). Scientists are still exploring the distribution and function of these subtypes of dopamine receptors, and there is evidence suggesting that each subtype of dopamine carries out a different function in specific regions of the brain. Interestingly, the dopamine D₂ receptor site appears to serve a regulatory function, controlling the dopamine subtype levels in various other parts of the brain (Murphy, 2012).

Researchers have indicated that individuals with reduced levels of dopamine D₂ receptors might be less sensitive to normal reinforcers such as food, water, and sex (Ivanov et al., 2006; Murphy, 2012). Compounds that force more dopamine into these receptor sites would in theory increase the level of neural activation to a more normal level, which would be experienced as rewarding by the individual. This theory is supported by the observation that cocaine administration increases the level of dopamine in such regions of the brain as the nucleus accumbens¹⁴ by 400–500%, while dopamine levels drop below normal in the nucleus accumbens during cocaine withdrawal (Ivanov et al., 2006). Thus, research is increasingly pointing to the importance of dopamine, especially the D₂ subtype, as a common element in the evolution of the SUDs (Brown et al., 2010; Murphy, 2012). However, “dissecting causality in studies of addiction is especially difficult because of multiple factors: genetics, early experience, acute pharmacological actions of misused drugs, potential neurotoxic effects of the drugs themselves as well as the effects of withdrawal, and long-term chronic effects of relapse and abstinence” (Everitt & Robbins, 2016, p. 35). Thus, even in interpreting what are considered major findings in the field, we cannot be sure if the changes are because of the SUD or if they caused the individual to seek drugs out in the first place (Everitt & Robbins, 2016).

NEUROIMAGING STUDIES

It has become possible to peer into the working brain through the use of neuroimaging equipment. One such study was carried out by Goldstein and Volkow (2002). The authors tried to identify a difference(s) between those with an SUD and those who did not have an SUD by measuring the levels of neural activity in the brain and found that the orbitofrontal cortex and the anterior cingulate gyrus, both of which are interconnected with the limbic system, become active when the individual misuses a compound. These regions of the brain are thought to be involved in the process of integration of goal-directed behavior and motivation. It was hypothesized that repeated exposure to drug-use cues would lead the individual to learn to expect certain effects from the use of a

¹³It should be kept in mind that the original studies were conducted on rats and not human subjects, and extrapolating from animal studies to human behavior is not always possible.

¹⁴This region of the brain is involved in the reward cascade.

chemical, while s/he also becomes less and less responsive to normal reward experiences. The authors suggested that individuals with an SUD might over-value the reinforcing effects of a substance, which when no longer present causes them to focus time and energy in an effort to reacquire these rewards. While this theory is still in its formative stages, it does appear to account for many facets of the SUDs. Trafton and Gilford (2008) also found evidence of altered neural function in such regions of the brain as the amygdala, the orbitofrontal cortex, the ventral tegmental area, and the locus ceruleus.¹⁵ While the authors suggested that these changes account for the behaviors seen in individuals with a physical addiction to a drug(s), it is possible that the observed differences *predate* the development of the addiction and are not the result of it, a problem highlighted by Everitt and Robbins (2016). There is obviously a need for further research into this topic.

DIGESTIVE SYSTEM

The possible interaction between the brain and the human gastrointestinal tract was long ignored by mainstream medical researchers. This is surprising in that the gastrointestinal tract is the only organ system in the body to possess its own neural network¹⁶ (Carpenter, 2012; Young, 2012). The *enteric nervous system* is involved with unconscious perception of environmental threats, the individual's response to such perceived dangers, and the production of stress-induced hormones (Young, 2012). Scientists have now accepted that communication between the central nervous system and the gastrointestinal tract is bidirectional and involves the enteric nervous system, the **vagus nerve**¹⁷ the endocrine and immune-inflammatory systems, as well as through transmitter modulation (Ackerman, 2012; Furness, Callaghan, Rivera, & Cho, 2014; Hornig, 2013). This suggests the possibility that the enteric nervous system might be involved in the risk assessment of substance withdrawal and possibly transmits this information to the brain for evaluation and behavioral response. There is an emerging body of evidence that there is a relationship between the intestinal flora¹⁸ and the release of dopamine in the brain (Lambert, 2015). Clinically this makes sense since the gastrointestinal tract is affected by both alcohol and drug misuse as well as by the process of detoxification from drugs.¹⁹

It is now believed that the normal balance of bacteria within the gastrointestinal tract, in combination with the body itself, forms a "super-organism." Many species of bacteria in the gastrointestinal tract produce neurotransmitters such as serotonin,²⁰ acetylcholine, and melatonin, compounds that in the brain are involved with the process of memory formation, mood, and learning (Ackerman, 2012; Carpenter, 2012; Davidson, 2014; Young, 2012). Researchers have even discovered that intestinal flora influence brain growth and development in mice. These findings hint that the bacteria in our gastrointestinal tract influence biological functions elsewhere in the body. Conceivably, there could be an interactional process between the intestinal flora and the substance use disorders.²¹ Human beings share 99.9% of the estimated 20,000 to 25,000 genes found in the human genome, so there is relatively little genetic variation between individuals. Yet the genetic makeup of intestinal bacteria can vary by as much as 90% between healthy individuals, although the strains of bacteria found in the gastrointestinal tract of any single healthy individual tend to be stable over the course of years if not decades (McGowan, 2012). This might explain the paradox that if one twin is alcohol-dependent, the odds that the other twin will also be alcohol-dependent are only about 50-50: They do not share the exact same gastrointestinal flora balance.

Many of the species of microorganisms in the gastrointestinal tract have co-evolved with humans over tens of thousands of generations, and it is unrealistic to think that the human and the gut microorganisms evolved separately from each other. The impact of substance use disorders on the body's normal balance of bacteria is also not well understood. It is known that heavy drinking alters the normal bacteria balance in the mouth, throat, and gastrointestinal tract (Engel, Green, Voigt, Forsyth, & Keshavazian, 2015), while methamphetamine misuse results in alterations and disruptions in the production of saliva and the body's ability to resist infectious diseases, the latter being caused by gastrointestinal microorganisms (Rommel et al., 2016). Conceivably these alterations might cause or contribute to behavioral changes in the individual misusing substances, although this is only a theory at this time. The role of bacteria in the development of eating disorders such as anorexia or obesity is also being questioned (Lambert, 2015). Given that the strains of bacteria normally found in the individual tend to be stable over the course of years, could the changes in gastrointestinal bacteria growth patterns found in individuals who misuse substances be part of why they crave drugs or alcohol after achieving abstinence?

¹⁵Essentially regions of the human brain involved in executive functions, and the limbic system, which is involved in the reward process.

¹⁶Comprised of approximately 100 million neurons embedded in the wall of the gastrointestinal tract (Carpenter, 2012) known as the enteric nervous system (Young, 2012).

¹⁷See Glossary

¹⁸A term that incorporates all of the microorganisms in the gastrointestinal tract.

¹⁹This is, however, a hypothesis on the part of the author of this text and has not been investigated by clinical researchers.

²⁰Ninety-five percent of the serotonin in the body is found in the gastrointestinal tract (Barbaro et al., 2016).

²¹This theory is only speculation on the part of the author, however.

The theory that infectious disease might be associated with psychiatric disorders is also now gaining widespread acceptance among scientists, although the research to date has yielded mixed results. Currently it is thought that at least some forms of psychiatric disease are the result of an autoimmune response triggered by exposure to an infectious disease (Hornig, 2013). The author speculated that the inconsistent findings found in past research might reflect differing levels of exposure to the causal agent, differences in the timing of the host to the infectious disease, or differences in the immune response between individuals who were exposed to the same disease (Hornig, 2013). It is not unreasonable to suppose that diet is one of the environmental forces that might contribute to the individual's vulnerability to an SUD. This is only a speculative hypothesis at this time, but one that does offer a novel treatment approach to the addictions if this theory is supported by further research.

Applications of the Biological Component of the Bio/Psycho/Social Model

The central tenet of the biological model of disease states is that information generated by research is then used to develop treatments to treat these conditions. The SUDs are considered disease states and are treated as such by proponents of the biological theory of addictions. Such treatment has taken four general routes. First there is the pharmacotherapy route, whereby physicians attempt to alleviate the distress associated with the withdrawal process. Many of the medications used in this process are intended for other conditions, and it is only by coincidence that they help with the withdrawal from alcohol or other drugs. A second approach has been to develop pharmaceuticals that might moderate or eliminate the individual's desire to misuse drugs (for example, methadone or naltrexone). A third approach has been to recruit the body's own defenses against drugs that have been misused (Giles, 2008). Experimental vaccines that prime the immune system to attack cocaine and methamphetamine molecules in the circulation appear to offer promise (Kosten et al., 2014; Kosten & Kosten, 2016) as does recent research on an analog of Modafinil®, a medication usually used in treatment of narcolepsy (Zhang et al., 2017). The vaccines will recruit the immune system into attacking the cocaine or amphetamine molecules while they are still in the circulation but before they reach the receptor sites in the brain. Theoretically, this would eliminate the reward potential for further misuse and make the individual more receptive to psychosocial interventions that are currently the mainstay

of substance rehabilitation. Finally, there is the promise that carefully selected psychosocial interventions such as cue exposure response therapies might work in parallel with biological interventions to increase the individual's chances of achieving and maintaining abstinence (Naqvi & Morgenstern, 2015), thus illustrating the interconnectedness of the various elements of the bio/psycho/social model.

An additional approach being explored within the framework of the medical model is the sequencing of the individual's genome to identify individuals at high risk for the development of a substance use disorder so that these individuals might be targeted for intervention. The exact form of such intervention remains unclear at this time. Some clinicians believe that it might be possible to alter the individual's genome to reduce their risk of developing a substance use disorder. Identified problem genes that contribute to the development of substance use disorders might be replaced by more benign genes, at least in theory. An alternative approach would be the development of pharmaceutical agents that would block the expression of the identified genes, again theoretically reducing the individual's risk for developing a SUD. These "treatments" are on the far horizon and might not be realized for generations, although the rapid progress in genetic engineering suggests that these interventions might become a reality in the next generation or two.

Reactions Against the Biological Component of the Bio/Psycho/Social Model

Philosophical

What do we mean when we say that something is a "disease"? The minister Robert Harris suggested that addictions were disease states in 1619, for example (Heyman, 2011). One must ask whether the meaning of the word "disease" has changed in the 500 years since Reverend Harris classified addictions as a disease state (Heyman, 2011). Is a disorder classified as a disease in the early 17th century the same as a disease in the 21st century?²² Does the identification of an individual as having a substance use disorder offer the clinician scientific or prognostic information of value in treating the person misusing substances, or are they just pseudoscientific labels (Bentall, 2009; Frances, 2013)?

If we attribute the individual's substance use disorder *only* to their genetic heritage, then we must absolve them of

²²For example, what might be "diagnosed" as demonic possession in the year 1620 might be diagnosed as Tourette's syndrome today.

responsibility for behavioral choices that they make (Frances, 2013). The individual's genetic heritage helps shape what a person finds rewarding. However, it is generally the individual's *choice* to indulge in these experiences or not (Greenstein, 2012). Another challenge to the medical model of the addictions is based on the oft-repeated statement that the substance use disorders are chronic, relapsing disorders. Thankfully, this is inaccurate: The substance use disorders remit at double the rate of other psychiatric disorders (Heyman, 2009).²³ This difference raises questions about the comparison between persistent medical conditions and the SUDs, although this fact is quietly ignored by proponents of the disease model as an inconvenient truth.

Methodological

Although initially embraced with great enthusiasm, animal-based research studies in the field of the addictions have become suspect. Data drawn from research conducted on animals does not simulate the human condition, making it difficult to generalize from animal research into much more complex behaviors such as a substance use disorder in an individual (Koob, 2008). The animals in the studies do not willingly ingest the compounds under circumstances that simulate the normal human's daily environment. It is not uncommon to learn that the animal was either forced to ingest the compound being tested or had it injected into their bodies.²⁴ Indeed, there is evidence that if placed in an enriched environment,²⁵ or if placed in a cage where they had access to substance-tainted and regular water from different sources, the animal's substance use is markedly reduced (Abadi, Miladi-Gorji, & Bigdeli, 2016).

Reactions Against the Jellinek Model

Many researchers have come to question the Jellinek (1960) model. The methodology on which Jellinek (1960) based his theory would now be viewed as flawed for several reasons: First, he mailed out 1,600 surveys to members of Alcoholics

Anonymous (AA). Of these 1,600 surveys, only 98 were returned (a response rate of just 6%). Few research studies today would be carried out on such a limited participation rate. Second, Jellinek (1960) assumed that AA members were the same as nonmembers. This is a dangerous assumption: By the very fact that they attended AA meetings, participants had identified themselves as being different in at least one respect from nonmembers. Third, Jellinek (1960) assumed that those participants who returned his surveys were the same as those who did not return his survey. However, in the very act of returning their survey, the 6% who did so marked themselves as being different from the 94% who did not return their survey.

The Jellinek (1960) model used a cross-sectional design. While this does not violate any known research rule, cross-sectional studies might not yield the same results as a lifespan (longitudinal) research design. For example: Did 50-year-old men with an alcohol use disorder begin to drink for the same reasons that 20-year-old men with an alcohol use disorder began to drink? The Jellinek (1960) model has not been found to accurately predict alcohol use patterns over the course of an individual's lifetime (Vaillant, 1995). Further, the idea of automatic progression in the severity of the individual's drinking has been challenged: The typical individual with an AUD alternates between periods of problematic alcohol interspersed with periods of less problematic use or total abstinence (Schuckit, 2006b; Vaillant, 1995; Willenbring, 2010). Individuals who misuse illicit drugs also tend to follow a variable course rather than an automatic downward spiral (Toneatto, Sobell, Sobell, & Rubel, 1999).

Another central tenet of the Jellinek (1960) model, that the individual will experience a *loss of control* over his or her alcohol use, has also been challenged (Heyman, 2009; Schaler, 2000). There has been no research suggesting that alcohol or drugs that are misused alter the voluntary motor control regions of the brain (Alquist & Baumeister, 2012). The individual's behavior may then be voluntary, as evidenced by the fact that individuals with an AUD drink in such a manner as to achieve and *maintain* a desired level of intoxication. Clinicians now speak of the individual as having *inconsistent control* over his or her substance use. There is little if any evidence that alcohol dependence is automatically progressive (Willenbring, 2010). It would thus appear that clinical research has repeatedly failed to support the Jellinek (1960) model, although it continues to strongly influence substance use theory and rehabilitation.

Genetic Inheritance Theories

The average person in the United States has almost been "programmed to believe [that] genetics rule" (Lipton, 2008, p. 186). The average person views his or her genetic heritage

²³Heyman (2011) suggested that by age 40, 50% of persons who once met the diagnostic criteria for alcohol dependence and 78% of those who once met the diagnostic criteria for another form of substance dependence no longer meet the diagnostic criteria for these conditions.

²⁴Admittedly, many individuals who use substances do inject drugs into their bodies. However, nobody asked the mouse or rat in the research study if they wanted to be injected, raising questions about the applicability of such research to persons with an SUD.

²⁵A large cage where there are other rats to interact with, toys to play with, grooming by laboratory staff, and places in their environment to explore such a cage with multiple levels, as opposed to being in a sterile cage with nothing to do but look at the walls or push a lever to get the occasional microinjection of cocaine, for example.

as inalterable fate (Watters, 2006), a process known as “neurogenetic determinism” (Begley, 2007, p. 252). An extreme interpretation of this position is that the person is then absolved of responsibility for their behavior, since they did not select their genetic inheritance! In reality, scientists have yet to agree on even such a simple concept as the definition of the gene (Moore, 2015). There is a general consensus that the individual’s genetic inheritance *influences* but does not control behavior (Gelernter & Kranzler, 2008; Moore, 2015). However, there is a bidirectional flow of information from the individual’s genes and their environment (Moore, 2015). This genetic influence is perhaps most clearly seen in the individual’s height. Although the individual’s genetic inheritance accounts for approximately 80% of their height, nutrition and the individual’s health status in the first two years of life appear to account for the other 20% of the variability in height.

For decades, researchers have cringed when people begin to speak of a hypothetical “alcohol gene.” The folly of this line of reasoning is readily apparent. There is, after all, no “fastball” pitching gene, or a “scuba diving” gene, so why should a disorder as complex as alcohol dependence rest on a single gene (Heyman, 2009; Nurnberger & Bierut, 2007)? Current research suggests that, like most behaviors, the addictions are *polygenetic* in nature. Perhaps 89 different genes are linked to substance dependence (National Institutes of Health, 2008), and the expression of these genes is strongly influenced by epigenetic changes. We do not understand which biological or environmental factors are necessary to induce or inhibit gene expression (Foroud & Phillips, 2012; Moore, 2015; Tattersall, 2012). As a result of these discoveries, many researchers now believe that the individual’s genetic heritage might account for as little as 10% of their risk for developing a substance use disorder (Rappaport, quoted in Hamzelou, 2011).

Consider the humble honeybee: All female honeybees develop from larvae that are genetically identical. However, only those larvae fed a special food known as “royal jelly” will grow to become a queen bee, while the others simply become sterile workers (Young, 2008). While human beings are a bit more complex than honeybees, this example does illustrate how external forces (in this case diet) influences the expression of the individual’s genetic heritage (becoming a queen or a sterile worker bee).

Another example of the fallacy of genetic determinism was clearly demonstrated in an experiment discussed by Tabakoff and Hoffman (2004): A number of genetically identical rats were sent to researchers in different laboratories around the country. The rats then received carefully calibrated doses of alcohol under closely controlled conditions. To the surprise of the researchers, the rats in the various laboratories demonstrated significantly different responses

to the same alcohol dosing regimen. The researchers began to investigate why and discovered significant differences in the environment in each laboratory where the rats were housed. In some laboratories, the rats were housed in sterile individual cages, while other laboratories housed the rats in individual cages with access to toys (what is often referred to as an “enriched” environment). Some laboratory workers did not touch the rats in their care per the protocol for that laboratory, while other laboratories encouraged the staff to pick the rats up, pet them, and in some cases allowed the rats to interact in a large communal cage with toys and interesting corners to investigate. All of these genetically identical rats received carefully calculated doses of alcohol at predetermined times, and promptly failed to respond consistently to alcohol in the anticipated manner. The results of this study were interpreted as evidence of how the environment influenced gene expression.

An additional complicating factor is that those genes involved in helping to initiate substance use might not be the same genes involved in the process of *maintaining* these behaviors (“Addiction and the problem of relapse,” 2007). Does the individual’s genetic heritage predispose him or her to begin to misuse chemicals, continue to misuse chemicals, both, or neither? The influence of the genetic inheritance upon behavior, or environmental forces on **gene expression**,²⁶ are simply not known, and for these reasons it is premature to point to genetics as a major factor in the evolution of a substance use disorder. We simply do not know enough about the role of genetic inheritance to make such generalizations . . . yet.

Reactions to the Epigenetics Model

We know so little about epigenetics that any statement that the addictions cause permanent changes in the brain is premature. It is possible that the substance use disorders do induce permanent changes in cellular DNA expression. Emerging evidence does suggest that with sustained abstinence at least some of these changes are potentially reversible. Scientists, as noted above, have yet to agree upon such a basic concept as what constitutes a gene, must less understand how the process of epigenetics might alter gene expression. While the discovery of epigenetics does offer potential insights into the SUDs and their treatment, it is far too early to predict how epigenetics will alter our understanding of the substance use disorders.

The discovery that there is an interaction between the individual’s genetic heritage and their environment through the process of epigenetics is an exciting discovery that potentially

²⁶ See Glossary.

could explain much about the addictions²⁷ (Starkman et al., 2012). Unfortunately, the relevance of epigenetics to the substance use disorders is not known at this time. The theory does appear to have face validity and researchers might very well discover that suspected epigenetic changes do influence substance use behaviors.

However, and this is the crux of this section, we just do not know enough about epigenetics to make definitive statements that epigenetic changes in genetic expression are involved in the substance use disorders. The critical periods of development are theoretical and not established fact, although, again, this theory has high face value in the opinion of the author of this text. There is a need for further research into the applications of epigenetic theory to the substance use disorders. Such research should help delineate the exact role that epigenetic changes play in the initiation and maintenance of substance use disorders, and whether the same epigenetic changes contribute to the individual's decision to initiate substance use as opposed to maintaining them, etc.

Reactions Against the Dopamine D₂ Receptor Site Hypothesis

The dopamine D₂ receptor site hypothesis seems to be the most promising of the medical models in explaining both the addictions and impulsive behavior in humans. Animal research suggests, for example, that rats that are deficient in the dopamine D₂ and D₃ receptor sites appear to be at increased risk for cocaine misuse (Dalley et al., 2007). However, much remains to be discovered about the distribution of the dopamine D₂ and D₃ receptor sites in the general population, the influence of a hypothetical deficiency of dopamine D₂ and D₃ receptor sites on behavior, and how behavior influences dopamine D₂ and D₃ receptor site status. Surprisingly, *social status* influences the number of dopamine D₂ receptor sites (Volkow & Li, 2009), which is an illustration of how environmental factors influence genetic predisposition. There is clearly a need for further research into the role of the dopamine D₂ and D₃ receptor sites on behavior and the prevalence of dopamine D₂ and D₃ receptor site deficiency.

Biological Vulnerability Studies

Marc Schuckit's (1994) study, on which the *low level response theory* is based, is frequently cited as evidence that there is a biological predisposition toward an alcohol use disorder. The results of this study are suggestive. However,

it should be noted that only 91 men in the original research group of 227 men had the abnormally low response to alcohol in the 1994 study. Of this group, 56%, or just 62 men, had progressed to develop an AUD at the time of the follow-up study. While this study does illustrate a possible biological predisposition for an AUD, it also demonstrates that this biological predisposition does not *predestine* the individual to develop the AUD. Many individuals with the same abnormally low response to the test dose of alcohol at the time of the initial testing did *not* have an AUD at the follow-up study.

Research support for the low level response theory has been mixed (King et al., 2011). For a subgroup of drinkers, alcohol appears to have a stimulant effect when their blood alcohol levels are still rising, a characteristic that King and colleagues (2011) found to be predictive of future binge drinking and eventually of future alcohol use problems. The authors speculated that low level responses observed by Schuckit (1994) might have reflected individuals' response to alcohol when their blood alcohol levels were dropping and not while they were increasing, raising doubts about the accuracy of the Schuckit (1994) study (King et al., 2011).

Challenges to the Neuroplasticity Aspects of the Disease Model

Advocates of the medical model are quick to point to **neuroplasticity**²⁸ as evidence that the addictions are biological disorders. Proponents of this position suggest that the repeated use of a recreational drug causes the neurons in different regions of the brain to *permanently* alter their structure and function, to the point where the individual no longer can exercise free will (Geppert, 2008). A counter point is offered by Heyman (2009), who suggested that "drug-induced brain change is not sufficient evidence that addiction is an involuntary disease state. Drugs change the brain, but this does not make addiction a disease" (p. 97). The neurons in the brain are constantly rewiring themselves to form new neural networks in response to life events and learning (Insel & Cuthbert, 2015). Diet, exercise, and even learning to play a musical instrument all induce changes in the structure of neurons in the appropriate regions of brain, but this does not make them "diseases." Further, the process of neuroplasticity might be active both in the development of and recovery from the substance use disorders (Torregrossa & Kalivas, 2009). We just do not know enough about this process to make definitive statements about the role of neuroplasticity in the substance use disorders.

²⁷Such as why, if one member of a pair of identical twins has an alcohol use disorder, the probability that the other twin will develop an alcohol use disorder is approximately 50-50, for example.

²⁸See Glossary.

Challenges to the Brain Imaging Studies

Proponents of the medical model will often point to dramatic brain scan pictures obtained from neuroimaging studies in which certain regions of the brains of persons with an SUD become very active when they are exposed to drug-use cues as evidence that the addictions are brain disorders. Some rehabilitation centers have used such brain imaging studies to purportedly demonstrate to the individual and his or her family that the individual is indeed addicted to chemicals and that changes in the individual's brain imaging studies over time reflect the positive impact of rehabilitation programs. This process ignores the fact that while neuroimaging studies are valuable research tools, they do not demonstrate the existence of a mental disorder,²⁹ or even diagnose them (Fletcher, 2013). No psychiatric disorder can be diagnosed solely by brain scans (Breggin, 2008). This is especially true for the substance use disorders: People are not referred to alcohol or drug rehabilitation programs because of an abnormal PET or fMRI scan (Peele, 2010).

However, the average person does not understand the process of neuroimaging, or that it is very easy to read too much into brain scans (Noe, 2009; Peele, 2010; Satel & Lilienfeld, 2013; Shermer, 2008). Stated very simply, neuroimaging studies do not reveal *what* the individual was thinking, only that certain regions of the brain appeared to be more active when they were thinking (Satel & Lilienfeld, 2013). Siegel (2013) arrived at a similar conclusion, stating: "[S]tatements that these scans were enabling us to 'see the mind in action' seemed like enthusiastic overstatements of the truth. After all, is blood flow change a measure of the mind? And what is the mind? Is the mind merely the activity of the brain?" (p. xix).

Yes, fMRI images are dramatic and look impressive. However, the average person does not understand that the images from brain scans are based on data obtained from individuals placed in an atypical environment: Being crammed in a neuroimaging machine and being exposed to photographs of drug-use cues is hardly the same as being in a street environment where the individual might be exposed to drug-use cues (Shermer, 2008). The resulting image is recorded on thousands of pixels, each of which reflects the average level of electrical activity from not just one or two but thousands of neurons (Yudste & Church, 2014). It is assumed by researchers that if certain regions of the brain

demonstrate evidence of increased activity when the individual is exposed to drug-use cues, this is evidence that the addictions are "brain diseases." The fact that there are some individuals who are known to be addicted to a chemical but who do not demonstrate activation of these same regions of the brain (Volkow & Li, 2009) is rarely discussed. Thus, the assumption that cerebral blood flow patterns are more complex than a simple person-views-drug-use-cue = increased-blood-flow to certain regions of brain reflecting preoccupation with substance use paradigm is poorly supported by the clinical literature at this time (Sirotin & Das, 2009). Changes in the cerebral blood flow patterns might take place in *anticipation* of expected visual stimuli, not in response to it (Sirotin & Das, 2009).

The layperson is also usually not aware that the dramatic colors produced by neuroimaging studies are based on apparent contrasts in the measured level of neural activity in various regions of the brain. One region of the brain might appear very active on neuroimaging studies because the level of neural activity in adjacent regions of the brain was *suppressed*, not because the target region of the brain is more active (Lilienfeld, Lunn, Ruscio, & Beyerstein, 2010). The average person is also rarely aware of the fact that the dramatic color differences that supposedly reflect levels of neural activity in different regions of the brain seen in **fMRI**³⁰ images are *artificially constructed* by technicians based on the study data (Legrenzi & Umiltà, 2011; Satel & Lilienfeld, 2013; Vul, Harris, Winkelman, & Pashler, 2009). Such images do not reveal the level of neural activity in regions of the brain adjacent to the one under study, even if the level of neural activity is only fractionally lower than those highlighted by the technicians. Another challenge to the neuroimaging studies of individuals who misuse substances has concerned the statistical analysis methods of the study, which might inflate the apparent level of neural activity, thus distorting the study's conclusions (Giles, 2009; Legrenzi & Umiltà, 2011; Noe, 2009).

There is also the rarely mentioned fact that neuroimaging studies are unable to determine what the individual is *thinking* (Horstman, 2010). Neuroimaging studies using the fMRI procedure have demonstrated that many of the same regions of the brain active in persons who relapse in response to a drug-use craving are also active in the brains of persons with a SUD who are experiencing a drug-use craving *but who do not give in to it*. Yet another confounding factor is that procedures such as fMRI do not provide real-time measures of brain activity (Frances, 2013). The images require several seconds to build up enough data to produce an image. During this time, the neurons in that region of

²⁹Although it should be pointed out that a consensus about the nature of mental *health* acceptable to all disciplines that address issues pertaining to the "mind" has yet to be suggested (Siegel, 2013). Given this fact, how can we as mental health or substance use rehabilitation professionals diagnose "mental illness"?

³⁰See Glossary.

the brain being studied have fired hundreds or even thousands of times in response to internal and external stimuli (Noe, 2009). Can we say with any degree of confidence that the measured level of neural activity was *all* in response to drug-use cues? Further complicating the application of neuroimaging procedures to the study of the substance use disorders is the fact that the images presented in textbooks and at public discussions are usually statistical compilations of a number of individual brains, not the representation of a single individual's brain activity (Horstman, 2010; Shermer, 2008). Thus, while brain imaging studies present researchers with powerful new tools for looking into brain function, it is far too soon to draw conclusions about what the findings mean. Neuroimaging is barely out of its infancy (Satel & Lilienfeld, 2013). To start making such dramatic claims as have been made in the popular press would be similar to announcing that a child will be a world-class runner after he or she took their first tentative steps. In both situations, it would be best to wait and see what develops.

Challenges to the Genetic Modification Treatment Approaches

At this time, knowledge about the genes possibly associated with a substance use disorder remains theoretical and is of little practical value to the clinician (Meyers & Dick, 2010). Before such attempts are made, it would be wise to consider the possibility that attempts to alter the expression of individual genes, or combinations of genes, thought to be associated with a substance use disorder are fraught with danger. First, the same genes might carry out multiple roles within the cell, depending on the order in which they are activated or deactivated, and we know virtually nothing about this process. Genes function more like a movie script than a blueprint, and the expression of genes can be modified or blocked by epigenetic changes initiated by person–environment interactions (Moore, 2015). We simply do not know enough about the human genome to safely make such changes to the individual's genetic inheritance. Like Murphy's law, the “**law of unintended consequences**”³¹ is always at work. There are always unanticipated consequences.

The Medical Model and Individual Responsibility

A central tenet of the medical model is that an *urge* to use a chemical is a compulsive, *uncontrollable* desire to use drugs that *must* be satisfied. This is simply not true for two reasons

(Alquist & Baumeister, 2012; Baumeister, 2015; Heyman, 2009; Satel & Lilienfeld, 2013). First, theories about the uncontrollable nature of an “urge” or drug-use “cravings” are based on reports from people who did not successfully resist these desires to use chemicals. We rarely receive feedback from those who *were* able to resist the urge to return to chemical misuse. Second, this perspective exonerates the person with an SUD from personal responsibility for his or her substance use (Baumeister, 2015). An interesting study carried out in the United Kingdom, briefly discussed in Baumeister (2015),³² suggested that volunteers working with those struggling with addictions tended to express the belief that the person remains in control of his or her behavior, while those individuals who were financially compensated for working with persons with an SUD tended to believe the opposite. The issue of individual responsibility in those persons with substance use disorders thus remains to be resolved.

Second, in spite of its characterization in the popular media, research has repeatedly demonstrated that the individual with an SUD does not lose the power of self-control (Alquist & Baumeister, 2012; Baumeister, 2015; Satel & Lilienfeld, 2013).³³ Substance-use cravings or urges are one of a number of factors that might trigger a relapse, but they are “not an obligation” (Heyman, 2009, p. 111) to do so. Any person who has been on a diet can testify that, while difficult, the urge to snack can be resisted. Many individuals struggling with addictions will admit that they can indeed resist the urge to use a compound *if the reward for doing so is high enough*. This introduces an element of free choice into a biological model that holds that free will is not a part of the disease process. It is the “elephant under the rug” of the living room that nobody wishes to acknowledge, although free will has been there all along.

Consider the following hypothetical example of an individual with a heroin use disorder who must (a) perceive the need for the drug, (b) obtain the funds with which to buy the desired drug, (c) find a supplier, (d) complete the financial transaction to buy it, (e) find a safe place in which to prepare the heroin for injection, (f) mix the powder with water,³⁴ (g) heat the mixture in a teaspoon, (g) put it into a syringe, (i) find a vein into which to inject the mixture, and then (j) inject the drug into his/her body. This is a rather complicated chain of events, each step of which involves the active participation of the individual. The hypothetical individual discussed here will pass through multiple decision

³¹See Glossary.

³²Unfortunately, Baumeister (2015) did not provide a citation for this study in his paper.

³³Who, for example, has ever heard of somebody running *into* a burning building to get a drink?

³⁴The assumption here is that the heroin is to be injected.

points requiring active participation on his or her part, but the person is then said to be a “victim” of the disease process. If we had to go through all of these steps to become ill, it is doubtful that anybody would ever be sick again!!

This places the medical model of the addictions in a quandary: What to do with free will? Philosophers are generally split into two camps: Determinists hold that all particles follow paths predetermined by the influence of every other particle in the universe³⁵ (Tse, 2013). Indeterminists adhere to the uncertainty principle and the laws of quantum mechanics to argue that all events are random. Individual decisions are the outcome of one of a number of neural pathways that might be activated when a decision is to be made, and are thus expressions of free will. On a behavioral level, O'Brien (2011) attempted to reconcile this apparent conflict by suggesting that the individual *initiates* the substance use, making the start of the addictive sequence a conscious choice. However, at some point this theory holds that substance-induced biological changes negate free will and the individual becomes a slave to his or her addiction. This attempt at reconciling two apparently diametrically opposed ideas overlooks the inconvenient realities that only a small percentage of those who experiment with alcohol or drugs do become addicted (Hari, 2015) and that a significant percentage of those who are addicted to chemicals do eventually learn how to discontinue substance misuse.

In the medical field, it is now accepted that the individual's behavioral choices, which are themselves reflections of free will, influence the course of a persistent disease state such as diabetes or the addictions. The individual may choose to follow medical recommendations, which may result in minimizing or totally negating the effects of his or her disease. This underscores the interlocking aspect of the bio/psycho/social model. If a hypothetical patient with adult onset diabetes were to lose 10% of his or her body weight, join a health club to exercise on a regular basis, and make certain changes in his or her diet (all social or behavioral choices), he or she would change the course of the disease. The same logic applies to the individual who has a substance use disorder: They remain responsible for the behavioral choices they make in response to this knowledge and its possible treatment (Washton & Zweben, 2006).

Unfortunately, the blind application of the biological model to disease states, including the addictions, appears to induce a mindset in health care professionals, psychologists, social workers, and the general public's view of a disease as an external entity that invades the individual, negating him or her to nothing more than the disease itself (Gunn, 2003).

In part, this is a reflection of the medical model of disease states, which prevents human contact by placing one person into the role of the physician and the other into the role of the patient (Frattaroli, 2001). This is rather disempowering, and one must ask how an impersonal medical relationship can ever hope to assist in the very personal and often painful disease state known as the addictions. In other words, the admonition made by Sir William Osler quoted at the beginning of this chapter is totally ignored. The health care professional now treats the disease entity (substance use disorder, cancer, neurological disorder, etc.) and not the person.

Spontaneous Recovery

Another challenge to the biological model of the addictions is *spontaneous recovery*. The prevailing opinion among physicians is that persons with substance use disorders are “exempt . . . from our beliefs about change. In both popular and scientific models, addiction is seen as locking you into an inescapable pattern of behavior” (Peele, 2004a, p. 46). However, in reality, “quitting is the rule, not the exception” (Satel & Lilienfeld, 2013, p. 55). While not every person with a substance use disorder resolves, it has been estimated that up to 75–95% of those with a SUD eventually do so,³⁶ either on their own or with professional assistance (Heyman, 2011; Marano, 2012; Satel & Lilienfeld, 2013; Willenbring, 2010). The spontaneous remission rate for SUDs is many orders of magnitude higher than that for other psychiatric disorders and raises serious questions about the loss of control that is supposedly a hallmark of addiction.

Section Summary

Modern biology has provided strong evidence that there are genetic predispositions toward substance use disorders. Brain imaging studies have found that there are increased levels of neural activity in specific regions of the brain when the individual is presented with images of their desired compound of misuse. However, it has also been demonstrated that there is an increase in neural activity in many of the same levels of the brain when the individual is actively thinking about *not using* the compounds pictured. The science of neural imaging has simply not progressed to the point where such distinctions are possible. Finally, although medical practitioners are quick to point to epigenetic changes within the brain as proof that the substance use disorders reflect a “brain disease,” there is an emerging body of evidence suggesting that with continued abstinence many of these epigenetic changes reverse

³⁵Through gravity, and possibly other forces.

³⁶The majority of those who recover from substance use disorders do so without going into treatment.

themselves. Thus, until the mysteries of epigenetics are unraveled, it is too soon to embrace these changes as proof that the addictions are brain disorders.

II. The Psychological Components of the Bio/Psycho/Social Model

Definition

The psychological component of the bio/psycho/social model explores the impact of psychodynamic forces, learning, motivation, interpersonal interactions, and personality on the individual's substance use behaviors (Sadock et al., 2015). This perspective is deeply interconnected with the biological and sociological components of the bio/psycho/social model. The individual's personality, which is both shaped by individual–environment interactions and helps shape future interactions with the environment, rests on a foundation of biochemical interactions within the brain. There are various theories within the psychological perspective on the substance use disorders, many of which are intertwined with the other two components of the bio/psycho/social model of the addictions. The application of the psychological sciences to various forms of psychological/psychiatric disorders is discussed in more detail in the chapter on co-occurring disorders; however, some of the more significant of the theoretical psychological models will be discussed below.

The Moral Model

One of the first psychosocial models proposed, one that still has many adherents among the general public, is the *moral model* (Brust, 2004). The moral model can trace its roots back at least to the “demon rum” philosophy on which the temperance movement of the 1800s was based. Proponents of the moral model view the addictions as reflecting a weakness of character. The “moral model” was applied not just to the substance use disorders such as alcoholism, but to a wide range of physical diseases. Bynum (2012) briefly discussed how it was assumed by many in the late 19th century that persons who contracted tuberculosis (TB) did so at least in part because of a vague, ill-defined, moral failing on their part, for example. Over the course of history, the list of medical disorders attributed to a character flaw on the sufferer's part has been quite lengthy. As applied to alcohol, this model would indicate that the individual succumbs to the temptations of alcohol (or by extension, illicit drugs) because of this unidentified but preexisting character flaw. There is a strong element of predestination inherent in this model: The person

did not select his or her moral character and thus is not entirely responsible for his or her attraction to alcohol. This belief is clearly seen in the result of a recent study conducted by Schomerus, Matschinger, and Angermeyer (2006). The authors interviewed 1,012 adults living in Germany by telephone and found that 85% of those who participated in the study thought that the addictions were a self-inflicted disorder, and only 30% thought that they could be effectively treated (Schomerus et al., 2006). Satel and Lilienfeld (2013) were more optimistic, noting that research data finding widespread support for the moral model has been mixed, but apparently the moral model of the substance use disorders has strong advocates in some segments of society.

Learning Theory

Learning theory suggest that the SUDs are a *learned* response to internal or external stimuli. The process of learning begins virtually at the moment of birth, and under normal conditions the human brain constantly seeks new knowledge and experiences (Suddendorf, 2013; Walter, 2013). This search explodes exponentially once the individual learns to speak, since words offer a way to categorize, think, and reason in a manner similar to those of our social group (Suddendorf, 2013).

Unfortunately, life experiences might be either positive (praise from parents, for example) or negative (being forced to watch violence between parental partners, for example). The strength of the learning process is perhaps best seen in the language-acquisition process. At birth the child does not possess a language (as we use the term), and even by the first birthday it is the exceptional infant who is able to utter a single word (Walter, 2013). By the age of 18 months the child is thought to learn a new word every two hours, and by adolescence the once wordless infant is learning 10–15 new words a day (Walter, 2013). The process of language acquisition begins at first in the parent–infant interactions that make college-educated adults sound like babies (“say da-da,” or “say ma-ma”) and gradually grows to include siblings, peers, social media, educational establishments, and the written word. This form of learning takes place in an interpersonal environment, often by listening to others and how they use a specific word in their everyday lives (Walter, 2013).

In this interpersonal matrix, the individual is exposed to substance-use cues of various intensities, which offer opportunities to engage in experimental substance use. For those individuals who become addicted to a chemical(s), their SUD appears to reflect a “maladaptive form of learning somehow etched permanently into the most primitive areas of the brain” (Piore, 2015, p. 44). Cigarette smoking provides an excellent example of the social learning process.

The smoker-initiate must first live in an interpersonal environment that, if not encouraging, is at least accepting of cigarette smoking. Then they must overcome their body's initial response to the chemicals in cigarette smoke, often because friends are there to help the new smoker learn why admitting so many poisons into your body is such a good thing. These friends provide role models that the new smoker might emulate. Once the new smoker has passed through the phase of nausea and vomiting, he or she will discover that they need to continue to smoke to avoid nicotine withdrawal, a matter that falls mainly in the biological part of the bio/psycho/social model (although psychosocial support during the process of quitting should not be dismissed).

In theory, the same mechanism is at work when the individual misuses alcohol and/or illicit drugs: Substance-induced pleasure reinforces the learning process and forestalls withdrawal distress, both of which then encourage further substance use. Its reward potential is strongest when its effects are unpredictable (Fiorillo, Tobler, & Schultz, 2003). In retrospect, this is obvious: Imagine the enthusiasm with which you would play a slot machine in Las Vegas if you were to win a consistent amount of money every time you played. You would quickly become bored and look for something else to entertain you. Very few people who misuse substances engage in the use of only one compound at the same dose. They often intermix chemicals, doses, or periods of time when they use a compound(s) to achieve variety in their drug use experience.³⁷ This phenomenon might also explain why illicit drug users keep using substances where the purity is not known: The effects of each substance misused cannot be predicted in advance, thus providing an element of the unknown for the individual.

Yet another form of learning takes place when the victim of extreme trauma finds that the use of alcohol and/or illicit drugs provides at least temporary relief from trauma-related distress (van der Kolk, 2014). Whether alcohol or drugs are misused for pleasure or for relief from trauma-related distress, the substance use disorders could be viewed as reflecting maladaptive learning (Lewis, 2011).

Coping Systems Theory

Coping systems theory overlaps with the social learning perspective in that alcohol and the drug(s) of misuse are viewed as becoming a coping mechanism for persons who suffer from depression or another severe psychological disorder. Psychoanalytic theorists have suggested that individuals

use alcohol or drugs to numb themselves to emotional pain (Dodes, 2013; Frattaroli, 2001; Hari, 2015; Horney, 1964; Maré, 2010; van der Kolk, 2014) or to self-medicate anxiety disorders (Encenaz et al., 2009). An intermediate theory has been advanced by Wise and Koob (2014), who suggested that at first, substance use is motivated by the pharmacological reward potential of the substance(s) being misused,³⁸ but that once tolerance develops, the individual's continued substance use becomes motivated by the desire to avoid withdrawal distress.

Personality Defense Theories of Substance Use Disorders

This theoretical construct draws upon both the psychoanalytic view of personality defenses and psychological personality theory. We are all thought to react to information about ourselves that we do not wish to face by unconsciously using one or more defense mechanisms. These defense mechanisms protect the individual from a perceived threat to his or her ego, albeit at the expense of long-term adjustment. Proponents of the psychoanalytic model have repeatedly asserted that persons with an SUD overuse individual-specific defense mechanisms because they keep people from feeling what they fear the most. "[T]he core of addiction doesn't lie in what you swallow or inject—it's in the pain you feel in your head" (Hari, 2015, p. 166). To avoid facing that pain, the addicted person hides behind a wall of drugs, according to the psychoanalytic perspective.

According to the *characteristic defense mechanism theory*, the most prominent defense mechanisms used by individuals with a substance use disorder are those of denial, rationalization, projection, and/or minimization. Unfortunately, the belief that individual misusing substances will automatically lie about his or her substance use pattern has become enshrined in clinical lore, as evidenced by the following quotation: the "use and abuse of alcohol and illicit drugs has long been associated with denial and misrepresentation" (Vitacco, 2008, p. 44). One of the most deeply entrenched beliefs among clinicians and the average person is that the individual with an SUD hides behind a wall of denial (Croft, 2006). Essentially, **denial** is a form of unconscious self-deception, which is classified as one of the more primitive, narcissistic defenses (Sadock et al., 2015). The conscious

³⁷Their choice of substances to misuse is affected in part by the *availability* of chemicals to misuse, which is discussed in greater detail in Chapter 37.

³⁸The compounds being misused are, from this perspective, being misused for their ability to bring relief from the psychiatric disorder that causes so much distress. A secondary effect of these compounds is their ability to initiate the reward cascade, although the author of this text has worked with individuals who claimed never to have achieved any sense of euphoria, but just relief from their mental illness.

mind simply refuses to acknowledge something that is threatening to the ego (Sadock et al., 2015). The analogy of “tunnel vision” might not be inappropriate here. The person allows the self to see only that which supports his or her desire(s) and avoids recognition of those things that do not support the desire(s): Threatening information is just dismissed. The individual’s use of denial might be illustrated by a hypothetical case in which a patient is informed by his or her physician that “the test results are back. I am afraid that the results were positive: You have cancer.” The individual might reply, “No, you’re mistaken.” The doctors are mistaken, they mixed up the blood test results, the test results were altered by the individual’s ingestion of an herbal medicine, etc. The process of denial might also be seen in the hypothetical person with an AUD whose spouse asserts, “You have a drinking problem!” The common reply is frequently, “No I don’t, I can control it. I can quit whenever I want to.” In the mind of the person with the SUD, the problem is solved: It just disappears (at least in his or her own mind), and evidence to the contrary is ignored or dismissed.

Another personality defense that is often seen in persons with a substance use disorder, according to clinicians, is **projection**. As the name would suggest, projection is a defense mechanism in which material that is unacceptable to the “self” is projected onto others (Sadock et al., 2015). The young child’s cry of “See what you made me do!?” is not a bad example of this defense mechanism in action. The child projects responsibility for his or her misbehavior onto others to avoid being held accountable for his/her misbehavior(s). In many cases, it is hypothesized, people misusing substances justify their abuse of a chemical(s) because they are the helpless victim of mistreatment at the hands of another, leaving no choice but to resort to alcohol or the illicit substances, that they are a helpless victim of their genetic heritage, past abuse, etc. On occasion, the drugs of misuse *do* serve this function, and the differentiation between those persons who are using projection to defend their addiction from those who are using a chemical(s) to help them cope rests on the skill of the assessor(s).

Often, individuals will attempt to justify otherwise unacceptable behaviors through cognitive justifications, or **rationalization**. For example, a hypothetical 73-year-old person with an AUD might explain that “the reason that I drink today is that my grandmother used to rub vodka on my gums when I was an infant.” Admittedly, physicians often did make this recommendation in the first quarter of the 20th century to help dull the infant’s pain during the teething process: Ethyl alcohol can function as an analgesic. However, the typical mother would dip her finger into a glass filled with vodka and rub less than a quarter of a teaspoon onto the infant’s gums every few hours. It is hard to believe that this medical

treatment carried out 70 years earlier caused the individual to have an alcohol use disorder today! Another example of rationalization might be found in the case of a hypothetical person who has a severe AUD and who argues that moderate alcohol use is good for the cardiovascular system.³⁹ This attempt at rationalization ignores research suggesting that while *moderate* alcohol use might offer some health benefit to the drinker, *excessive* alcohol use can cause significant damage to the body. Thus, this defense mechanism allows individuals to justify otherwise unacceptable behavior (at least to themselves). Another commonly encountered rationalization is that marijuana is not dangerous since it is a plant, and how can naturally occurring plants be addictive or harmful?⁴⁰

The individual who uses **minimization** as a defense will either consciously or unconsciously reduce the incidence of a socially unacceptable behavior, or its effects on others. For example, one person might explain, “I only drink on the weekends,” but not offer the additional information that for them the “weekend” begins on Friday afternoon or evening, and lasts until late Sunday evening. Another person might admit to “experimental” use of cannabis, while his or her spouse reports that the partner smokes it three times a day, every day of the week. Further, the “I only had two beers” story that police officers often hear when they stop a suspected intoxicated driver might be viewed as an attempt at minimization.

Behavioral Psychology Theories⁴¹

There is no consensus about the definition of the “behavioral psychology” schools of thought. The question of whether this is a philosophy, a paradigm in which to view human behavior, or a therapeutic approach has yet to be resolved. The behavioral psychology theories are quite deterministic in orientation; however, behavioral therapists range from rigid, staunch believers in this philosophy through moderate behaviorists who accept the existence of basic biological drives such as hunger, thirst, and sex. To such theorists, the behavior of the organism is motivated by the desire to reduce the tension induced by unfulfilled biological drives such as those noted above. However, all behavioral therapists maintain that “personality” is simply an illusion, and avoid the “black box”

³⁹See Chapter 8.

⁴⁰Two counterarguments present themselves: First, tobacco is also a plant, and, as discussed in Chapter 16, smoking is a major cause of premature death around the world. So even “natural” plants can be harmful to the user. Second, both the tobacco and marijuana plants have been subjected to selective breeding experiments over the generations, the result being that the plant that emerged from these experiments is far more potent than the original plants found in this country generations ago, and are hardly “natural” plants.

⁴¹For purposes of this text, the behavioral theories are classified as a psychological school of thought.

of human thought, free will, or personality (Davies, 2015). Indeed, hard-core behavioral psychologists maintain that “the very idea of the ‘mind’ was just a philosophical distraction” (Davies, 2015, p. 96).

At the risk of gross oversimplification, the central tenet of behavioral theory is that humans, like all animals, work to either (a) increase personal pleasure or (b) decrease discomfort. These are called *stimuli* (singular: *stimulus*). The individual’s behavior in response to a stimulus is called a *response*. Behavioral therapists maintain that all behavior can be understood in terms of stimulus–response cycles. Things that (a) increase pleasure or (b) decrease discomfort are said to be *positive reinforcers* for that response. Behaviors that result in a (c) decrease in pleasure or (d) increase in discomfort are said to be *negative reinforcers* for that response. The influence of various reinforcement schedules⁴² on animal behavior in the research laboratory setting have been explored, and it has been observed that behaviors that result in a positive response induce the development of a *habit*, the strength of which reflects in part the reinforcement schedule that contributed to the development of that habit. The repeated failure of a given stimulus to elicit positive reinforcement or reduce punishments may result in the *extinction* of the identified behavior. The speed with which an identified behavior becomes extinct is dependent in part on the reinforcement schedule that initiated the development of that habit.

A simplified application of this model to the substance use disorders would suggest that it accounts for the behavioral patterns seen in persons with an SUD. Within this model, the substance use disorders are viewed as meeting either condition (a) or (b) above. However, repeated exposure to drugs can result in the individual becoming physically dependent on the drug(s) being used. At this point, the motivating force behind further substance use is to avoid either the loss of what is perceived as pleasure or possibly even going into a withdrawal syndrome—conditions (c) and (d) above. Obviously, the behavioral psychology reinforcement schedules appear to account for many of the phenomena observed in those who misuse substances; however, there are significant exceptions as well: the documented alcoholic who decides that the time has come to stop using alcohol and chooses to go through alcohol withdrawal, for example. So, while the behavioral psychology theories offer valuable insights into the motivation for substance use behaviors, they do not provide a “grand unifying theory” of the addictions.

⁴²The topic of reinforcement schedules on behavior is far beyond the scope of this text. The reader is referred to any of a number of excellent books on behavioral psychology theory to learn more about this topic.

Cognitive-Behavioral Theories (CBT)⁴³

The *CBT theories* emerged in the last quarter of the 20th century and reflect a modified form of the behavioral therapy approaches to treatment. The CBT theories do not address the issue of predestination, but focus on those patterns of thought that contribute to or support the substance use disorder in the here and now. Individual thoughts, feelings, or beliefs are accepted as being either rational or dysfunctional. Possible stimuli trigger dysfunctional thoughts or logic chains within the individual. An example of a dysfunctional thought might be the hypothetical individual’s belief that “nobody likes me” because of a lack of telephone contact with family or friends in the past week. There are many potential explanations for the lack of contact with family or friends, not the least of which is simple coincidence.

The goal of cognitive behavioral therapy is to (a) help the individual identify his or her thoughts in reaction to a specific event, (b) determine how these thoughts contribute to the individual’s emotional response to that event, (c) determine which thoughts are dysfunctional, (d) learn how to replace these thoughts with more appropriate responses to the event, and (e) monitor the efforts to replace these self-defeating thoughts with more appropriate thoughts. To extend upon the example outlined above, the client’s use of “black-and-white” thinking (“Nobody likes me!”) would be targeted, and appropriate treatment goals would be established to assist the client in addressing these maladaptive thoughts.

Psychoanalysis⁴⁴

Psychoanalysis is strongly deterministic in orientation. The individual is being both consciously and unconsciously motivated to engage in certain behaviors by past interpersonal relationships and unresolved conflict(s). In brief, this form of treatment calls upon the therapeutic relationship as the tool for behavior change (Horvath & Luborsky, 1993). However, many individuals who have developed an SUD have suffered so much abuse at the hands of significant others that it often is difficult if not impossible to establish the rapport on which the psychoanalytic relationship must rest. In successful therapeutic relationships, evidence would suggest that

⁴³Like every other therapeutic model reviewed in this chapter, this school of thought is far too complex to review in just a few paragraphs. The reader is referred to any of a wide range of books on the subject, including those by Albert Ellis or Aaron Beck, to cite but two of the many pioneers in this field.

⁴⁴Psychoanalysis was initially envisioned as a medical specialty, although many other professionals now engage in the practice of psychoanalysis after completing the appropriate training. For purposes of this text, this school of thought is reviewed in the psychological section of the bio/psycho/social model of the addictions.

the therapeutic relationship itself fosters neural reorganization (Cozolino, 2014). The process of developing a successful therapeutic relationship appears to trigger the process of neuroplasticity through a neutral but supportive client–therapist relationship (Cozolino, 2014; Feldstein-Ewing & Chung, 2013). Within this therapeutic relationship, learning occurs, altering existing neural networks (Feldstein-Ewing & Chung, 2013). For this reason, psychoanalysis can be viewed as falling across the full range of biological, psychological, and social realms of treatment.

The Addictive Personality

The theory of the “**addictive personality**” is strongly deterministic, as evidenced by fact that the “very word *addict* [which] confers an identity that admits no other possibilities” (Peele, 2004a, p. 43, italics in original). Drawing upon clinical experience with persons who were addicted to alcohol or drugs, a number of writers suggested that personality traits such as impulsiveness, thrill seeking, rebelliousness, aggression, and nonconformity were “robust predictors of alcoholism” (Slutske et al., 2002, p. 124). Clinicians began to look for evidence that clients in their care possessed at least some of these personality characteristics, and not surprisingly concluded that their clients did have at least some of the personality traits outlined above. These therapist-based conclusions then reinforced the theory that there was an addictive personality in the minds of some therapists.

Applications of the Psychological Component of the Bio/Psycho/Social Model

Assessment

The psychologist is often in the unique position of being able to assess the individual’s intellectual and personality resources and areas of vulnerability. The psychologist and others working with those struggling with addictions have the opportunity to determine the individual’s motivation for substance use. Individuals with posttraumatic stress disorder (PTSD), for example, might drink or use illicit drugs to make themselves numb when memories of the traumatic situation threaten to break through to their consciousness. Other victims of PTSD might drink or use illicit drugs to give themselves the right to vent long-repressed feelings. There are individual-specific reasons why a given individual might misuse alcohol or illicit drugs, placing the helping professional in the unique position of determining why a client has an SUD.

Psychologists may also be in the position of guiding a treatment team to design a personalized treatment plan for each client. Substance rehabilitation for a hypothetical person who has a measured IQ of 80 would proceed down different paths than a rehabilitation program for a person who has a measured IQ of 115, for example. Personality assessment might reveal that a certain person is overly dependent on others, or suspicious of others, both characteristics that will influence the course of a rehabilitation program.

Neuropsychological Assessment

This is a specialized application of the psychological assessment process. The neuropsychological assessment is carried out to determine whether certain life events such as involvement in a motor vehicle accident have influenced a person’s ability to understand and adjust to their environment. The neuropsychological assessment will reveal the *level* of impairment, if any, the functions that are impaired (language recognition as opposed to the ability to do math problems, for example), and provide an overview of remedial services that may be needed for the individual.

Individual or Group Psychotherapy

Persons who struggle with a wide range of mental health problems often benefit from concurrent individual or mental-health group psychotherapy sessions as part of their rehabilitation program. In many cases, the individual will discuss issues with their individual therapist that they would never reveal in a therapy group setting. Many of these sensitive issues contribute to or help sustain the individual’s substance use, and some of the major schools of thought related to therapy were discussed earlier in this chapter.

Cognitive Dissonance

This is a phenomenon seen when an individual is confronted with information that conflicts with established beliefs or ideas. This creates a sense of unease or discomfort within the individual. This reflects our ongoing attempt to reconcile expectations with reality. Imagine a cave man or woman who believes they can see the face of a predator hidden in the nearby grass. This is the expectation: Predator!!! If another cave man or woman were to say that it was only an illusion created by light and shadows that they have seen several times in the past few days, this creates the phenomenon of dissonance: I have to see for myself before I dismiss it. This investigation then reconciles the conflict between expectation and experience. Cognitive dissonance is also easily demonstrated in substance rehabilitation programs: The individual’s experiences with a drug has been essentially

positive in many ways. Now treatment staff are attempting to convince the person that drug use is wrong, that it contributes to familial conflict, etc. The conflict between these two positions is easily seen. Unfortunately, individuals faced with cognitive dissonance often try to resolve the conflict by simply avoiding situations where they are likely to be exposed to information that might increase the dissonance and thus their psychological distress. In other words, the probability is high that they will either drop out of treatment, give the illusion of participation without intending to challenge their beliefs, or fail to attend recommended community-based support groups upon discharge.

Professionals working with those struggling with addictions should keep this phenomenon in mind, and might even use it in the individual's treatment program. Asking the person who holds the belief that "I can control it" to go two weeks without *any* alcohol use causes the individual to confront his or her belief of self-control with personal experiences, for example. The danger in using this approach is that if the individual succeeds, he or she will interpret this as evidence that treatment is not needed, or if he or she fails in this task, may choose to simply drop out of treatment (thus avoiding the conflict between the belief that he or she can control substance use and the reality of his or her failure to do so).

Marital and Family Therapy⁴⁵

Many health care professionals are trained in the art of marital and family therapies. An adjunct to substance rehabilitation programs might involve marital and/or family therapy to help family members learn how to deal with issues such as how anger is expressed within the family unit, abuse from significant others, child discipline, financial decision making, sexual relations within the marriage, and the anger that partners feel about the substance use behaviors.

Although clinical wisdom suggests that those with severe substance use disorders have alienated themselves from family and peers who might have provided a source of support, this belief has not been empirically tested. The possibility exists that for an unknown percentage of those who misuse substances, it might be possible to affect a reconciliation with family members or peers who might eventually become sources of support for the individual. The possibility also exists that the family or the marital partner might

prove detrimental to the individual's efforts at recovering from his or her substance use disorder. While it is the goal of the marriage and family therapist to achieve the former goal, he or she must also constantly assess the progress of the therapeutic process and help the person in the early stages of recovery to achieve distance from those members of his or her family who are unsupportive for reasons of their own SUDs, unresolved anger issues, or other reasons that are intractable to therapy.

It is regrettable that while the psychological theories of addictions offer valuable insights into the forces that initiate and maintain the SUDs, they do not provide a grand unifying theory of the addictions. Another perspective also offers valuable insights into the substance use disorders: the social theories, which are discussed later in this chapter.

Reactions Against the Psychological Models of the Substance Use Disorders

Reactions to the Moral Model of the SUDs

The scientific foundation for the moral model is weak at best; however, it still has strong adherents among the general public (Brust, 2004). One of the goals of Jellinek's (1960) work was to eliminate prejudicial judgment of persons with alcohol use disorders by demonstrating that they had a medical illness. It is hard to judge whether this goal has been met: More than a half century after Jellinek's work was published, Pescosolido and colleagues (2010) found staggering rates of prejudice against those persons with AUDs. However, it is not known whether the rates of prejudice uncovered by Pescosolido and colleagues (2010) were higher than, equal to, or lower than those that existed at the time that Jellinek (1960) conducted his research.

One of the strongest challenges to the moral model is that it is more than two hundred years old and was advanced well before the process of neurotransmission or regional specialization centers in the brain had been discovered. To illustrate the influence of time, consider that it was suspected that the person who contracted tuberculosis (TB) was thought to have done so because of a moral shortcoming, until the science of infectious diseases revealed that TB was a bacterial infection. The very age of the moral model does not make it responsive to new discoveries about human motivation, or how personality disorders might predispose the individual toward a substance use disorder, for example. It is suggested that the moral model is an antique best relegated to the history books.

⁴⁵The author recognizes that marital and family therapies do not fall exclusively under the umbrella of the psychological sciences and that social workers and many addiction counselors also engage in this adjunctive therapy after receiving special training for this difficult task. However, for the sake of this text, marital and family therapies will be discussed in the psychological sphere of the bio/psycho/social model.

Reactions to the “Alcoholic” (or “Addictive”) Personality Theories

Although long established in clinical lore, the theory of the “alcoholic personality” is nothing more than a clinical myth (Gendel, 2006; Stetter, 2000). According to this theory, clinicians are trained to expect certain personality characteristics in persons with an alcohol use disorder, and then selectively recall only those cases that meet these expectations.⁴⁶ If this theory is true, then one of the cornerstones on which substance rehabilitation is based is flawed. However, clinicians continue to operate on the assumption that their clients are (a) developmentally immature, (b) motivated to hide behind certain personality defenses such as denial, and (c) tend to be impulsive. Treatment is then geared to address these perceived personality flaws in the client, whether they exist or not. Further, the personality profiles of persons with alcohol use disorders were based on studies involving persons in treatment for their AUD. This raises the question of whether what was being measured was an “alcoholic personality” or a “treatment personality” (Pihl, 1999). Research continues to look into the personality characteristics that seem to overlap with addictions, but some call for removal of this term from treatment professionals’ vocabularies, since the concept lacks sufficient research support and causes “confusion and misunderstanding and undermines our ability to help individuals” (Amodeo, 2015, p. 1031).

In the face of this lack of supporting evidence, one must ask how the myth of the alcoholic personality evolved. One theory is that clinicians and researchers in the mid-20th century became confused by the high rate of comorbidity between individuals with a substance use disorder and individuals with an antisocial personality disorder (ASPD). This is understandable, since between 84 and 90% of males with ASPD will also have an SUD at some point in their lives (Preuss & Wong, 2000; Ziedonis & Brady, 1997). This is not to imply that the ASPD *caused* the SUD or the reverse! Rather, they are separate, coexisting conditions, with each interacting with and affecting the course of the other. Given that individuals with ASPD demonstrate many of the personality traits attributed to the addictive/alcoholic personality, it is easy to understand how one came to be confused as being synonymous with the other.

Challenges to the “Characteristic Defenses” Theory

The assertion that persons with an SUD overuse certain defense mechanisms has been repeatedly challenged. Indeed, there is evidence suggesting that the belief that individuals

with a SUD will *automatically* rely on the defense mechanisms outlined earlier in this chapter might do more harm than good (Foote, 2006). Miller and Rollnick (2002) suggested, for example, that *as a group*, persons with an alcohol use disorder do not use denial more frequently than any other group. Fletcher (2013) noted that persons with an SUD are likely to be honest about their substance use patterns if they have little reason to fear that the information they provide will be used against them later. If one assumes that this is true, then the myth of client denial of substance use problems might at least in part reflect client defensiveness about possible prosecution if they reveal too much about their past.

However, because of selective perception by the therapist(s), the myth that the person misusing substances will automatically use the defenses discussed earlier in this chapter was established. To support their thesis, Miller and Rollnick (2002) point to what is known as the “**illusion of correlation**.” The illusion of correlation suggests that we tend to remember events that confirm our preconceptions and dismiss or forget information that fails to do so. According to this theory, substance rehabilitation professionals are more likely to remember those clients who demonstrated the defenses of denial, rationalization, projection, and minimization. This selective perception overlooks the possibility that the client’s stage of growth and the treatment approach being utilized did not match, and not that the individual was in a state of denial (Miller & Rollnick, 2002).

Challenges to the Behavioral Psychology Theories of the SUDs

Detractors of the behavioral psychology theories of the substance use disorders have mounted a spirited assault on what is otherwise a well-established motivational theory. The Institute of Medicine (2015) issued a report citing the limited research evidence on the effectiveness of the cognitive behavioral therapies as one reason why private health insurance companies hesitate to reimburse therapists or agencies utilizing such interventions. This report also cited the limited number of therapists trained and certified in using cognitive behavioral interventions, and the fact that of this number an even smaller pool of therapists are willing to accept private insurance company or government health program reimbursement policy restrictions on their practice.

An interesting dilemma was presented by Baker, Stockwell, Barnes, and Holroyd (2011), who observed that a subgroup of their research sample was resistant to cognitive behavioral therapeutic intervention because of their depression.⁴⁷ An interesting question not addressed by this

⁴⁶The same process is seen in cases where other drugs of misuse are involved as well.

⁴⁷This study also illustrates how mental health issues frequently coexist in persons with substance use disorders.

study is whether their depression was a preexisting condition that prevented them from learning from experience (thus increasing discomfort in the long term), or if their failure to learn from experience contributed to their depression. Either way, the authors indirectly illustrate how the individual's state of mind influences their ability to learn, an issue that is apparently unique to the human species.

Criticism of the Behavioral Psychology Approach

A strong criticism of the behavioral psychology theories is that much of the early behavioral psychology research involved animals placed in artificial environments such as a cage fitted only with a lever. Each time the animal pushed the lever, he or she would receive a small reward (a food pellet, or a small dose of a drug like cocaine administered through an indwelling catheter, for example). Such research did indeed uncover the basic laws of behavioral psychology, and the animals in these studies behaved in a predictable manner: They would push the lever to receive the reward associated with that action. Various reward schedules were identified (continuous or 1:1 reinforcement paradigms, intermittent reward paradigms, or fixed ratio reward schedule paradigms, for example) through such animal-based studies. However, such studies ignored the fact that the animal was in an artificial environment. In the example noted above, the cage offered nothing more beyond the lever in the wall, limiting the rat's behavioral options to just using the drug being administered. In an "enriched" environment, the animal's dependence on drugs previously given is significantly less than for those in nonenriched environments, and actually show reduced withdrawal symptomology (Abadi et al., 2016). Given these details, one must wonder whether the animals' observed substance use in the early research was motivated by a desire to use chemicals or by sheer boredom.

A further challenge to the behavioral psychology schools of thought can be found in the discovery that the individual's frame of mind, a personality trait, can influence learning (Baker et al., 2011). A subgroup of their research sample consisted of a number of depression-prone individuals who were more resistant to learning from mistakes and more likely to continue counterproductive behaviors such as substance misuse. Studies such as that conducted by Baker and colleagues (2011) raise questions about the applicability of animal-based behavioral research to human behavior. Admittedly, many people continue to abuse chemicals in spite of social prohibitions, legal sanctions, and the discomfort of drug withdrawal. However, researchers have attempted to understand whether the perceived benefits outweigh the consequences of these behaviors *from the perspective of the*

person misusing substances. This raises the issue of individual choice in the behavioral psychology paradigm of the addictions, a confounding factor that must be integrated into a perspective that has contributed much to our understanding of addictive behavior.

Challenges to the Learning Theories of the SUDs

There has been little criticism of the learning theories, possibly because these theories do appear to account for many of the phenomena demonstrated by persons with substance use disorders. Also, learning systems theories overlap with the behavioral psychology and cognitive behavioral psychology paradigms, for example, which are reviewed elsewhere in this chapter.

Reactions Against the Coping Skills Theories

There has been remarkably little criticism of the coping skills theories, possibly because they are rather eclectic and are drawn from a wide range of other theoretical models.

III. The Social Component⁴⁸ of the Bio/Psycho/Social Model

Definition

Substance misuse does not take place in a vacuum: In contrast to the biological and psychological components of the bio/psycho/social model, this perspective attempts to identify and address those social forces that contribute to the individual's increased vulnerability to the substance use disorders and increase his or her compliance with prescribed medications (Batman & Miles, 2015).

Overlap with the Biological Model

The development of the brain is not guided just by the genetic potential of the individual. Rather, the human brain is also a social organ that, from the first days after birth, begins to absorb and respond to the rules of social interaction. This occurs first within the caretaker–child relationship, as the primary caretaker(s) attend or fail to consistently respond

⁴⁸The author has taken the liberty of using the words "culture" and "social" interchangeably.

to the child's cries for attention. These social interactions help to shape neural growth in different regions of the brain (Lieberman, 2013). *Touch* has been found to influence brain growth, both stimulating the child's developing neural development and providing the infant a sense of security through the warmth of the mother's body as she holds the infant and attends to the infant's needs. The impact of maternal neglect on the infant's neural development is just beginning to be investigated, but must certainly influence this process as well.

Surprisingly, within the first days following birth, the infant learns to initiate and maintain social interactions through his or her cries and the nature and duration of eye contact with those in the immediate environment. The infant might respond with apparent excitement when he or she sees a familiar face, maintaining eye contact until he or she feels sensory overload, at which point attention is turned elsewhere. Later, during the maturational process, the infant begins to study the faces of other people, exploring similarities and differences between the facial features of the caregiver(s) and those of new people they encounter.⁴⁹ The infant's response, a sharing of the "self," then initiates a social interaction as the "other" responds to the child's initiative. The infant's social interaction pattern is then shaped by those caregivers who most consistently interact with that infant.⁵⁰ This contributes to the infant's ability to tolerate stress, as evidenced by the observation that maternal anxiety results in the mother interacting with her infant less, becoming more withdrawn and disengaged from the infant at a time when the infant's brain is undergoing rapid growth in which the first neural pathways specific to social growth are being established (Nicole-Harper, Harvey, & Stein, 2013).

Although initially it is through the family that social mores are taught to the child (Eberstadt, 2013),⁵¹ the infant is rapidly exposed to other sources of social interaction and opportunities for observational learning⁵² (Cozolino, 2013). Initially the lessons that are learned through the social environment are often tempered by parental input ("I don't care what your friends say, skipping school is wrong and if you do it again you will be punished"). This process contributes to the "chaotic, astonishing, tumultuous stew we call human

culture" (Walter, 2013, p. 152). The discoveries of the child parallel and possibly contribute to the process of deteriorating familial bonds; the guidance that these bonds offer the developing individual have deteriorated to their weakest point in history (Eberstadt, 2013).

During childhood and adolescence, relationships influence the development of the cortex, which in turn provides the cognitive resources that the individual draws upon to learn the interpersonal skills necessary to function within society (Cozolino, 2013). This process begins within a closed social circle defined by family membership (caregivers and siblings, for example). As the definition of "family" blurs or possibly disappears through such processes as divorce, remarriage, out-of-wedlock childbirth, and single-parent childrearing, traditional sources of feedback to the child, sources which in turn influence neurocognitive development, are diminished or lost (Eberstadt, 2013).⁵³

The typical adult has five relationship levels. The infant starts life with one relationship level, the *first-order relationship* circle, usually defined through biological kinship ties (parents, siblings, etc.) (Gamble, Gowlett, & Dunbar, 2014). This relationship level usually consists of up to about five persons. However, children are biologically programmed to explore and expand their social world. They develop friendships outside the family circle, and these *second-order relationships* include approximately 15 individuals such as best friends and trusted role models. The interpersonal relationship pattern at this level is of less intimacy than first-order relationships. These individuals share many of the same interests and values, although there is a degree of fluidity in this group as the individual struggles to reconcile different sets of social values while maturing and coping with external events over which they have no control.⁵⁴ During the process of growth, the individual develops yet a larger sphere of *third-order relationships* consisting of about 50 persons. Examples of such relationships include other students, coworkers, neighbors, etc. The individual might share a few interests with these individuals but have less emotional investment with them than with those persons in second-order relationships (Gamble et al., 2014).

Fourth-order relationships involve persons with whom the individual's emotional social ties as well as shared values are weaker yet (Gamble et al., 2014; Suddendorf, 2013). Such social groups include between 150 and 500

⁴⁹It would be interesting to know how an infant views the facial features of a pet dog or cat as opposed to those of a human being, although it is doubtful that this question will ever be answered.

⁵⁰Whether the infant is being raised in an extended family, a single-parent family, as an oldest child, a middle child, or the youngest child, etc.

⁵¹Eberstadt's text *How the West Really Lost God* (2013) addressed the forces that contributed toward breaking the bond between the individual members of society and the established church. However, many of her observations do address the issues under review here, and for this reason are included in this text where appropriate.

⁵²Television programming for children is one example of this process.

⁵³Single parenthood, for example, often robs the child of feedback from a second set of grandparents, while divorce and remarriage might expose the child to conflicting feedback about social values from an acquired new family during critical periods of neurocognitive and neurosocial development.

⁵⁴A best friend might move with their family to a distant city or a beloved relative die, to cite two of a wide range of such factors.

individuals (Suddendorf, 2013). Members of a fourth-order relationship circle include casual acquaintances or persons with whom the emotional and social ties are still weaker (distant cousins, coworkers in another department, etc.). Finally, there are the *fifth-order relationships*, consisting of a sphere of about 1,500 persons that the individual is vaguely aware of but with whom social and emotional ties are weakest (Gamble et al., 2014). Ultimately, by adulthood we have participated in so many different social groups, and met so many other people through work or other organized social groups,⁵⁵ that we are enmeshed in a wide range of relationships that fall within the entire spectrum of social intimacy outlined above (Hecht, 2013).

This does not negate the influence of larger social groups such as the country in which a person lives; however, the individual's emotional and social ties to such megagroups are minimal.⁵⁶ The individual might belong to a political party and work as a volunteer for that party but have minimal social or emotional investment with other volunteers or members of that party. As the person becomes a fully self-sufficient individual, they are freed from the necessity of personally devising a response to each situation by calling upon the standards and lessons learned by members of lower social levels (Churchland, 2013).

On a systemic level, the sociological perspective of the substance use disorders attempts to identify and possibly correct systemic issues within society that might influence the individual's decisions about substance use, including the cultural, environmental, and familial elements of the individual's life (Sadock et al., 2015). These forces can either facilitate the development of a substance use disorder or contribute to the individual's resilience against the SUDs (Winters et al., 2012). Preliminary research suggests that extra support and nurturing for at-risk children and adolescents fosters the development of resilience within the child, although the identification of at-risk children and the proper forms of intervention remain elusive (Belsky, 2015). It is thus to a culture's benefit to identify those forces that foster the development of resilience while understanding and correcting problems that contribute to the development of the SUDs. To this end, the social sciences have much to offer society in its struggle against the substance use disorders.

The Role of Substance Use in a Culture

Virtually every known culture encourages the use of a select chemical(s) to alter the individual's perception of reality⁵⁷ (Glennon, 2008). Social factors that influence the individual's substance use decisions include (Pihl, 1999) (1) the general cultural environment, (2) the specific community in which the individual lives, (3) subcultures within the parent community, (4) family and/or peer influences, and (5) the context in which the compound is used. Further, the perceived *availability* of a given chemical(s) and the individual's *age* also influence substance use behavioral decisions, although these factors are often overlooked by researchers (Bennett & Golub, 2012; Latimer & Zur, 2010).

Engaging in the use of accepted substances under appropriate conditions serves several functions within a culture: It might facilitate social bonding, serve as a means of religious communion with the gods, or function as a form of personal recreation or as a form of rebellion by members of a subgroup(s) within the larger community, to cite but a few of the many roles that a substance might play in a given culture. The culture defines the meaning of the substance use, identifies behavioral rules by which its members are expected to abide, the sanctions for violating these norms, and the means by which those sanctions are enforced.⁵⁸ Unfortunately, cultural norms are extremely slow to change, frequently leaving the individual without guidance when faced with misinformation and misperception about appropriate substance use behaviors.⁵⁹

Individual substance use behaviors are influenced by additional three factors: (a) *drug* (including the method of administration and pharmacological reward potential of the substance), (b) *set* (the individual's expectations for the use of the chemical, personality characteristics, and current state of mind such as depression, suspiciousness, or feeling hopeless), and (c) *setting* (the context in which the substance use takes place). Arguably, "drug" might be said to fall within the purview of the biological sciences, while "set" falls under the umbrella of the psychological sciences. "Setting" addresses the more salient social forces that help to shape the individual's substance use behavior. In their examination of adolescent alcohol use by inner-city youth, for example, Epstein, Griffin, and Botvin

⁵⁵Being the coach or advisor of an after-school sports team such as a weekend baseball league and meeting with the parents of other members of the team, for example.

⁵⁶Soldiers fight, for example, often not for "God and Country," as the saying goes, but for friends with whom they have formed second-order relationships who might be in the next foxhole or assigned to the same duty in combat. Such activities might serve the purpose of the megagroup.

⁵⁷Before you begin to argue against this statement, consider the case of caffeine: How many of us would like to begin the day without that first cup of coffee or two (or three . . .) in your system? Remember: Caffeine is a chemical, too!

⁵⁸This is seen in how alcohol use by individuals in some Native American tribes is viewed as a sign of deviance, and these individuals are shunned, while group drinking is viewed as the norm and at least tolerated by members of the community.

⁵⁹Lest too many people become upset after reading this sentence, it should be noted that *abstinence* is also a substance use behavior: The individual chooses to abstain from the use of alcohol, tobacco, or illicit drugs.

(2008) observed that the perceived benefits of drinking and social opportunities (such as employment) are the two most robust predictors of actual alcohol use by inner-city adolescents.

These categories are not mutually exclusive but interact to help shape the individual's substance use behaviors. An excellent example of this interaction effect was observed toward the end of the U.S. involvement in the Vietnam conflict. It was clear that victory was unlikely, and large numbers of troops were being withdrawn from that country. Studies revealed that 45% of soldiers stationed in Vietnam were using heroin, which was of high purity, inexpensive, and plentiful. Follow-up research revealed that within a few months of their return to the United States only 5% of these individuals continued to use heroin (Hari, 2015). These findings illustrate the strong influence of "drug" (high-purity, low-cost, readily available heroin), "set" (loss of hope for victory), and "setting" (a military unit that was accepting of illicit drug use) interacted to influence individuals' substance use decisions.

Within the larger culture are various smaller social groups that reject at least some of the rules of the parent culture.⁶⁰ Those soldiers in the last paragraph who used heroin while stationed in Vietnam illustrate the development of subgroup-specific values that were at odds with established military protocol, to cite one example. Some of the other forces that influence the individual's behavior include his or her perceived position within a social group (influential or peripheral member) and perceptions of acceptable behavior(s) within that subgroup (Valente, Gallaher, & Mouttapa, 2004). It is possible that at least some of those soldiers who used heroin while they were in Vietnam did so because they perceived that this was the behavioral norm for the unit to which they were assigned, not because of any internal desire to use opiates. The relationship between various subgroups and the parent culture might be conceptualized as shown in Figure 26-1.

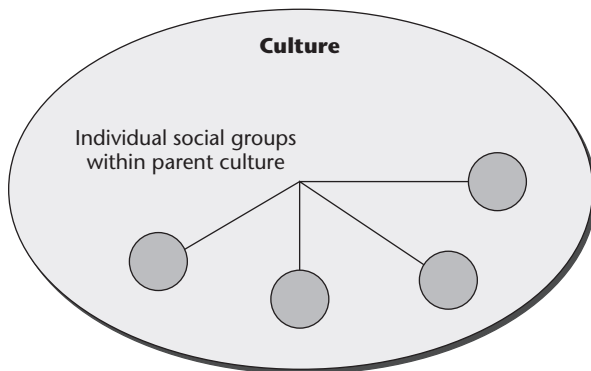


FIGURE 26-1 The Relationship Between Different Subgroups and the Parent Culture.

⁶⁰The religious group known to historians as the Puritans comes to mind here. They rejected the values of England to seek the right to practice their religion as they thought appropriate.

Through the process of social learning or social modeling, the individual participates in activities that define a subgroup (such as the abuse of certain chemicals, style of dress, shared interests in certain forms of music, etc.), all reinforcing the participants' identity as members of a given subculture (Bennett & Golub, 2012). However, it is necessary to remember that membership in one subgroup does not exclude participation in other subgroups or the parent society (Bennett & Golub, 2012). Those soldiers who were using heroin while stationed in Vietnam, for example, were still members of the military, and subject to the rules and regulations that govern military life, even if these rules and regulations were not rigorously enforced at the time.

Social Factors Influencing Individual Substance Use Decisions

In addition to the general influence of the social environment are a number of social factors that increase the individual's vulnerability to or help protect the individual from the substance use disorders. In this section, we will briefly review some of the most important of these social factors.⁶¹

ADVERTISING

Arguably one of the strongest influences on the use of those compounds that are legal to use, alcohol and tobacco products, is the advertising industry. This is demonstrated by the apparent correlation between the amount of money spent on tobacco product advertising and the number of children or adolescents who begin to smoke (Shadel & Scharf, 2012). The impact of advertising appears to be strongest prior to the initiation of cigarette smoking by children or adolescents, but after nicotine addiction develops advertising does not have the same impact on individuals' substance use behaviors (Shadel & Scharf, 2012). The influence of advertising on adult smoking or alcohol use is still not well understood at this time, but there is no reason to suspect that advertising does not influence smoking or alcohol use behaviors by adults.

ATTACHMENT BONDS

The formation of attachment bonds overlaps the psychological and biological fields. However, since the formation of attachments bonds takes place in a social environment it is examined as a social process.

Attachment bonds are those ties initially to the infant's parents or caregivers, and over time to a growing sphere of siblings, close relatives, etc. Infants are obviously dependent on the caregiver(s) following birth, and the development of

⁶¹Unfortunately, many of these social factors overlap. For example, parenting could be said to overlap with familial factors influencing substance use decisions. However, when in the author's decision a specific social factor warrants separate consideration it will be discussed even if it does overlap other social forces.

attachment bonds is an unconscious process that begins at birth. If the initial caregiver(s) are reasonably responsive⁶² to the child's biological and psychosocial needs in the first few years of life, that child will probably form positive attachment bonds to the caregiver(s). Issues that interfere with the caregiver's ability to properly interact with the infant or child, such as maternal substance use, illness, depression, or other severe forms of mental illness, will interfere with the formation of positive attachment bonds by the infant. These negative attachment bonds could potentially leave the infant with the expectation that others will not be responsive to their needs or desires, or even that others will be abusive and thus not worthy of trust.

Positive attachment bonds do not prohibit later substance use or misuse, although they do serve a protective function, reducing the possibility for the development of an SUD. Individuals with poor attachment bonds might find alcohol or illicit drugs a trustworthy source of positive feelings in spite of their early life experiences, increasing the possibility that the individual will develop an SUD later in life. Attachment bond reconstruction therapy is possible, but it is a prolonged process fraught with the risk for therapeutic misadventures.

COST

The economic investment in substance use often serves as a deterrent to alcohol use. Zhao and colleagues (2013) examined mortality statistics in British Columbia for the period from 2002 to 2009 and found that the government-mandated 10% increase in the minimum price of beer and distilled spirits resulted in a 32% drop in the number of deaths that were clearly alcohol-related, such as alcohol poisoning and alcoholic cardiomyopathy. The authors speculated that one reason for the observed drop in alcohol-related mortality might be that even heavy drinkers reduced their daily alcohol intake in response to the increased cost of their preferred beverages. This study is but the latest in a long series of studies that discovered an inverse relationship between the cost of alcoholic beverages and the amount of alcohol consumed. It is not known whether this inverse ratio between cost and substance use applies to the illicit drugs, although this would appear to be fertile ground for clinical research studies.

ENVIRONMENTAL FACTORS

The social environment can also provide the individual an awareness of the availability of drugs and alcohol and their effects (Johnston, O'Malley, Bachman, & Schulenberg, 2012b). In this manner, social ties might serve as a conduit to such information. Factors such as poverty, lack of social opportunities, lack of vocational opportunities, and familial structure then form the framework within which the individual makes

substance use decisions that will either facilitate or help protect the individual from substance abuse (Dunlap, Johnson, Kotarba, & Fackler, 2010). For example, in certain levels of society the sale and distribution of drugs is viewed not with disdain but as legitimate ways for the individual to quickly acquire wealth and prestige where other opportunities to do so are limited at best. It is not known whether these factors apply to the initiation of substance abuse, although there is firm evidence to suggest that children and adolescents tend to overestimate their peers' use of alcohol, tobacco, and other compounds, suggesting that they might overestimate the potential benefits of alcohol (and illicit drug) use, adding to their vulnerability to development of an SUD.

One surprising environmental factor, one that in this case overlaps with familial influences on substance use decisions, is the size of the family (Muschel, Ratner-Stauber, Marfolis, Demaria, & Schechter, 2013). The authors examined a sample of orthodox Jewish adolescents and found that individuals misusing substances were more likely to come from larger families than those who did not use. It is possible that larger families did not allow for the same quality or quantity of parent-child interaction, serving to isolate the child or adolescent from what would normally be a protective factor against substance use. Another potential factor, one that illustrates the interlocking nature of the biopsychosocial model, is how severe emotional and physical abuse stresses the body's adaptive resources, teaching the individual to expect more abuse, leaving the individual in a hypervigilant state in which the individual is constantly on guard for signs of potential harm (van der Kolk, 2014). In theory, many of these individuals might turn to misuse of alcohol and drugs to find relief from this constant activation of the fight-or-flight response.

EXPECTANCIES

The development of the individual's expectancies for the effects of various compounds is shaped, in part, by how the misuse of those compounds is portrayed by the media. In medicine this would be called the "**placebo effect**": A compound works because the individual *expects* that it will work. When a pharmaceutical company applies for permission to market a new compound, it must (among other things) demonstrate that it is more effective than a placebo. Unfortunately, the cognitive immaturity of children, adolescents,⁶³ and at least some adults makes it difficult for the person misusing substances to appropriately assess the benefits or risks associated with substance use, contributing to a tendency for many to overvalue the perceived benefits of substance use while downplaying the risks associated with this practice.

⁶²The "good enough" parent.

⁶³Discussed in Chapter 20.

HOPELESSNESS

Hopelessness overlaps the problem of victimization (discussed below) and is a robust predictor of substance misuse. This is demonstrated by the findings of Zhang and colleagues (2008), who concluded that the incidence of SUDs and mental health problems is higher in the less affluent regions of Appalachia. This is an ill-defined region of the country, but it has long been economically disadvantaged, offering residents few opportunities for social advancement, especially in those regions where the once predominant industry of coal mining has been curtailed and unemployment is higher. Hope for social and financial stability within this area is limited at best. The misuse of prescription drugs by teens and young adults has become rampant in Appalachia, although use of heroin and other illicit compounds is also not uncommon there. Alcohol as always plays a significant role in the substance use problem in this region, if only because it is so accessible.⁶⁴ As this illustrates on a regional level, the loss of hope contributes to vulnerability to the substance use disorders.

INDIVIDUAL LIFE GOALS

Identified life goals help to shape the individual's substance use behavior(s) (Alquist & Baumeister, 2012). Again, the influence of individual life goals upon the person's behavior begins to manifest during adolescence and becomes stronger during late adolescence and young adulthood. At each point in life, the individual must determine whether substance use or misuse is consistent with his/her long-term life goals. The more clearly defined the individual's life goals and commitment to achieving these goals, the less vulnerable they are to the development of a long-term substance use disorder (Alquist & Baumeister, 2012). However, the reverse is also true: If the individual's life goals are ill-defined, the individual's vulnerability to the initial temptation of substance misuse and the possible development of a long-term substance use disorder are correspondingly greater (Alquist & Baumeister, 2012).

Those individuals who constantly monitor their progress toward their life goals are less vulnerable to the temptations of substance misuse, especially when such behavior is contrary to the identified life goals. However, should the individual become unsure about his or her priorities in life, he or she becomes more vulnerable to the dangers of substance use (Alquist & Baumeister, 2012). Commitment to life goals is rarely a problem for semi-socially approved compounds such as alcohol and tobacco. However, consider a low-level business executive who is being considered for a major promotion in another company, but who discovers

that the potential new employer has a strict no-smoking policy. The individual then has a choice of either changing his/her smoking habits so that s/he could accept the new position, or rejecting the new job because of the no-smoking policy. A flow chart of the decision-making process that the individual went through might look like the one in Figure 26-2.

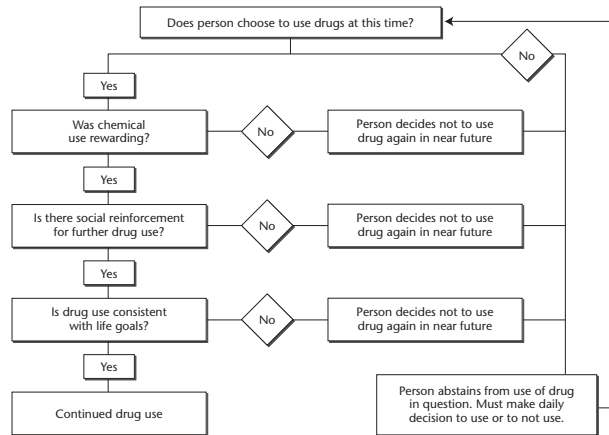


FIGURE 26-2 The Chemical Use Decision-Making Process.

Should this hypothetical individual have a clearly defined goal, say to be a mid- or upper-level administrator in his or her chosen profession by the age of 40, he or she must reconcile continued substance use with the possibility of achieving this goal. Losing focus on this life goal might make the individual more vulnerable to the temptations of substance use (Alquist & Baumeister, 2012). While the commitment to life goals will not entirely protect the individual from the dangers of developing a substance use disorder, it is one factor that lends impetus either toward or away from such a problem.

LEGAL SANCTIONS

Many of the legal sanctions imposed against those who break social rules governing substance use behaviors are well known and need not be discussed further in this section. A new issue, however, is the move by some states to charge persons with metabolites of THC in their system with the criminal offense of "driving under the influence (of chemicals)," even if the person is using "medicinal" marijuana. The judicial system has, broadly speaking, adopted the stance that any evidence of THC in the individual's blood or urine is grounds for legal action.⁶⁵ Further, a number of states have legalized recreational marijuana use. The legal system in each state struggles with these issues.

⁶⁴Arguably, the long history of illegal alcohol distillation and sales in this region of the country could be said to have provided tacit approval of other forms of substance misuse.

⁶⁵As opposed to alcohol levels in the person's blood: If the person's blood alcohol level is below the defined level (usually 0.8 mg/dl of blood), they are not charged with driving under the influence of alcohol in most cases.

MASS MEDIA

A surprising social factor that apparently contributes to substance use disorders is the media. The manner in which substance use, including that of alcohol and tobacco, is portrayed helps shape the individual's expectations for that compound's effects (Griffin & Botvin, 2010; Shadel & Scharf, 2012). After reviewing popular youth-rated movies released between 1996 and 2009, the team of Bergamini, Demidenko, and Sargent (2013) concluded that only 22 movies each year portrayed cigarette smoking, a decline from earlier decades, which the authors attributed to the Master Settlement Agreement of 1998, which resolved claims against the tobacco industry by various states. However, in the same period portrayals of or references to alcohol use increased from 80 a year in 1996 to 145 a year in 2009.

Sports or entertainment celebrities are frequently viewed as role models by children, adolescents, and occasionally by adults. This is shown by the sales of replica football jerseys: The majority of jerseys sold have the name and number of a favorite player, and only rarely is a second- or third-string player's name found on a jersey. The manner in which substance use is portrayed by the media, including music videos, also helps shape the individual's expectations about the degree to which the use of illicit drugs is acceptable (Griffin & Botvin, 2010). If a sports figure or media star were to be known to use a certain substance, this would to some degree "legitimize" the use of that compound, especially for adolescents. However, there has been little systematic research into this topic, and there is much to be discovered about the interaction between substance use by admired persons and individuals' substance use.

MEDICAL CARE

Although the treatment of disease states is reviewed earlier in this chapter, medical care does not exist in a vacuum. Various social factors such as financial stressors, living arrangements, employment, etc. influence the individual's access to and utilization of medical care services. In a study that overlaps the biological and social models of the substance use disorders, the Robert Wood Johnson Foundation (2011) found that four out of five physicians surveyed said they felt unequipped or untrained in helping patients address social problems that might contribute to their medical disorders. Thus, the lack of medical care integrated with psychological or social service supports limits the effectiveness of medical care and contributes to the tendency to misuse chemicals by some individuals.

MUSIC

Although often overlooked, music both helps to transmit social mores and provides behavioral models for the listener. The popular music of the 1950s frequently referred to marriage and lifelong commitment as appropriate goals. References to casual relationships were prohibited, or at least

censored, as evidenced by the refusal of many radio stations to play the song "Kisses Sweeter Than Wine" in the 1950s. The rationalization for this refusal was that the words were too provocative.⁶⁶ By the mid-1960s, indirect, carefully worded references to illicit drug use were included in the lyrics of many popular songs, and by the late 1960s and throughout the 1970s, popular music often expressed a casual "love 'em and leave 'em" theme (Epstein, 2012, p. 56).⁶⁷

The effects of music apparently are an unexplored element of the impact of music on the individual's social development. It is known that music stimulates the release of dopamine, and the nucleus accumbens becomes more active when the individual is listening to music, biological functions that parallel the individual's enjoyment of the music (Kalat, 2009). The majority of popular songs in the 1960s were in a major key, which, when combined with a fast tempo, tends to elicit positive moods in the listener (Epstein, 2012). By the middle of the first decade of the 21st century, the majority of the popular songs were written in a minor key, which tends to elicit sadness and depression in the listener (Friedman, 2012). These are emotions that, as discussed elsewhere in this text, encourage substance use in an attempt at self-medication.

PARENTING

The topic of parent-child relationship patterns is discussed in more detail in Chapter 20. However, the reader must be reminded that the parent-child relationship that evolves over the course of the child's development is a potent social factor that can either constrain, give tacit approval to, or even encourage substance use by the growing individual.

PEER GROUPS/SOCIAL SUPPORT

Although the influence of peer groups on the individual's behavioral choices is strongest during childhood and adolescence, peers still retain some influence over the individual in the adult years. These relationships also indirectly reflect the individual's own drinking status: "[I]n young adults," Lau-Barraco, Braitman, Leonard, and Padilla (2012) stated, "the proportion of heavy drinkers in one's social network predicts personal drinking" (p. 748). This effect appears to be strongest for men, although it applies to women as well (Lau-Barraco et al., 2012). These "drinking buddies" unconsciously shape the individual's drinking on specific occasions. Volkow, Frieden, Hyde, and Cha (2014) discovered that the individual's drinking partners influence their own drinking.

⁶⁶It is ironic that the lyrics to this song refer to a lifelong commitment to a spouse, and it is now broadcast without protest by many "easy listening" stations.

⁶⁷Arguably, this shift might be seen in the music of the band The Beatles over the years. A comparison of the content of their first songs with that of their final songs would arguably illustrate this shift in social values.

The individual's substance use decisions reflect a process of social learning (Lau-Barraco et al., 2012). The individual drinker unconsciously decides whether a person whose primary interest is the use of chemicals (Lau-Barraco et al., 2012) should fit into the circle of friends closest to them, from whom they will learn substance use behaviors, or if they should be relegated to one of the less intimate groups which each person surrounds himself or herself.

Surprisingly, global levels of positive social support appear to have a stronger influence upon the individual's behavior than do recovery-specific nonsupportive forces, possibly because the positive social support could enhance the individual's general feelings of competence and efficacy (Schmitt, 2003). Social support might fall into one of four different categories: (1) physical support (financial assistance or assumption of child care responsibilities for limited periods of time⁶⁸), (2) emotional support (unconditionally listening to the problems the person in early recovery encounters, or assisting the individual to form non-substance-centered friendships), (3) information sharing (to help the individual with unbiased decision making), and (4) feedback from others to the individual about their behavior (including possible early signs of a potential relapse, as well as what others perceive the individual is doing to help themselves). The positive form of any of these categories is supportive of abstinence from substance use, while the negative form of any of these four categories might contribute to the individual's ultimate relapse back into active substance use.

RELIGIOUS AFFILIATION

The individual's involvement with a formal religious group has been found to exert a deterrent effect on the individual's substance misuse and criminal behaviors (Koenig, Haber, & Jacob, 2011). This deterrent effect begins to manifest during adolescence and continues through adulthood. Koenig and colleagues (2011) identified several mechanisms through which religious affiliation might influence substance use behaviors and concluded that the (a) increased social support, (b) nondrinking norms, and (c) opportunity to gain relief from suffering all appear to influence alcohol use decisions by members of the religious community. Unfortunately, the deterrent effect might reflect a self-selection process through which those individuals most likely to engage in criminal behaviors or the misuse of illicit compounds avoid involvement with a formal religion. Still, there does appear to be a negative correlation between involvement in religion, especially *active* participation as opposed to simply attending services, and involvement in socially unacceptable behaviors (Koenig et al., 2011).

SEX RATIO

Guttentag and Secord (1983) advanced a controversial theory that the male:female ratio helped to shape cultural norms. The authors suggested that when there is an excess of available men as opposed to women, social values tend to be more conservative and supportive of traditional marital values, strengthening the role of marriage as a stabilizing influence in the society. When the number of available women is equal to or exceeds that of available men, social values shift toward the liberal end of the spectrum, according to the authors. On this theoretical basis, Epstein (2012) suggested that the social values for the next 25 years will tend to be more conservative, since the ratio of available men to available women will be approximately 1:1. This theory is quite provocative, and, obviously, there is a need for more research in this area.

SOCIAL MORES

An interesting social experiment has been taking place in Sweden. As the social restrictions against the use of tobacco products by women in that country relaxed, a greater and greater number of younger women were taking up the habit of smoking cigarettes (Kendler, Thornton, & Pederson, 2000). There is no evidence of a massive shift in the genetics of the population in that country as of yet, so it is logical to expect that cultural and social factors were acting as a balance to the desire of some women to smoke cigarettes. When these sanctions began to ease, the number of women in Sweden who smoked cigarettes began to increase. It is not unreasonable to say that social rules also strongly influence other substance use behaviors beyond that of cigarette smoking.

VICTIMIZATION⁶⁹

Researchers have found a strong relationship between childhood abuse and neglect by the parents and subsequent substance misuse when the child grows up (Chaffin, Kelleher, & Hollenberg, 1996). There is also a relationship between victimization through interpersonal violence and substance use disorders, as noted in Chapter 18. This is a bidirectional relationship, however, with some women who were victimized sexually turning to amphetamines or cocaine *after* the assault, while some individual's substance use disorder might predate the assault(s) (Gilbert, El-Bassel, Chang, Wu, & Roy, 2011).

It is not possible to identify every social factor that might contribute to the development of a substance use disorder. However, the list of factors identified above helps isolate some of the more pertinent social forces that can protect against or contribute toward the possible development of an SUD.

⁶⁸Or "babysitting."

⁶⁹This topic is worthy of a book in its own right, but we are forced to summarize the topic in just a few sentences.

Applications of the Social Component of the Bio/Psycho/Social Model

Griffin and Botvin (2010) suggested that the continuum of intervention into the substance use disorders involves three elements: (a) prevention, (b) treatment,⁷⁰ and (c) maintenance.⁷¹ Prevention, according to the authors, is further subdivided into (i) universal interventions, (ii) selective interventions, and (iii) indicated interventions. Universal forms of intervention focus on the general population, with the goal of avoiding or delaying the initiation of substance use. Selective interventions target identified high-risk groups, while indicated interventions focus on those individuals who demonstrate early warning signs suggestive of a possible SUD developing. Indicated interventions might be viewed as falling under the umbrella of the psychological sciences, again underscoring the interrelatedness of the bio/psycho/social model of the addictions.

One selective intervention reviewed by Griffin and Botvin (2010) was the Community Trials Intervention to Reduce High Risk Drinking (RHRD). This intervention model is based on five components, each designed to reduce potential high-risk drinking: (1) reduced access to alcohol through application of community zoning ordinances, (2) training those who dispense alcohol to recognize individuals whose alcohol use has put them at risk for driving after drinking, (3) application of law enforcement activities such as sobriety checkpoints aimed at drinking and driving, (4) training retailers to recognize underaged drinkers and refrain from selling alcohol to them, and (5) formation of community coalitions that will support and encourage the application of steps 1–4. One example of a community-wide or systemic intervention aimed at reducing high rates of alcohol misuse or use by minors are state-mandated increases in taxes on alcoholic beverages, which apparently resulted in a 32% reduction in alcohol-related deaths when implemented (Saitz, 2011; Zhao et al., 2013). Other systemic responses to the problem of alcohol use/misuse include limiting the number of outlets through which alcohol might be obtained, such as prohibiting the sale of alcohol except at state-licensed stores (Saitz, 2011).

Although the original intent of the paper by Tracy, Munson, Peterson, and Floersch (2010) was to identify social forces that might pressure a woman into or away from substance misuse, these factors could apply to either a male or female with a substance use problem. Emphasis on those positive social forces that impact the individual's recovery

from a substance use disorder offers the opportunity to increase the individual's chances of success. Identification of negative social forces so that these issues might be addressed will reduce the possibility of the individual relapsing back into, or continuing, the misuse of chemicals. These positive and negative factors are outlined in Table 26-1.

TABLE 26-1 Factors that Contribute to or Detract from Potential Recovery from an SUD

Positive Factors (Which Support Recovery Efforts)	Negative Factors (Which Undermine Recovery Efforts)
Emotional support	Preoccupation with problems others are experiencing (caretaking)
Encouragement	Ties to past substance centered support
Care and concern	("She used to baby-sit the kids when I went out to buy drugs," for example)
Communication (friends, family) Able to count on others for emotional support	Lack of support from social network (is made to feel guilty for past substance use, for example)
External support (checking up on person)	Lack of support from prior social network
Praise and recognition for hard work ("You have worked so hard to stay clean," for example)	(former "using buddies" who now work to undermine the individual's efforts to abstain from drugs)
Positive social encounters	Identification with substance-abusing subgroup for sense of belonging
Tangible help (child care, place to live, etc.)	Members of social group who keep reminding person of past trauma associated with substance use ("Have you met any abusive partners since you stopped drinking?")
Bringing personal items to person while in rehabilitation program (comb, shampoo scented soap, etc.)	
Keeping lines of communications open (telephone calls, greeting cards, letters, etc.)	Living in proximity to drug dealers or substance abusing "friends" visiting person attempting to abstain from alcohol or drug use
Involvement in social activities (going shopping with a friend, or meeting for lunch, etc.)	Physically abusive or substance-using significant other
Providing information and support of efforts to learn about effects of drugs.	Lack of assertiveness skills
Social skills training	

SOURCE: Based on Tracy, Munson, Peterson, and Floersch (2010).

⁷⁰Discussed in chapter 31 on treatment.

⁷¹Discussed in chapter on treatment.

Psycho-Educational Intervention Programs

The Drug Abuse Resistance Education (DARE) and similar programs are examples of social interventions and are quite popular, if of questionable effectiveness (Saitz, 2011). Such programs are based on the theory that by teaching children about the harmful effects of alcohol or drugs while helping them build self-esteem, this would inoculate them against the desire to misuse chemicals in later life. The DARE program is usually led by a local police officer, and is carried out in the classroom setting. Other programs utilize the services of various mental health or school guidance professionals. While there is a great deal of anecdotal support for such programs, there is only limited clinical research data suggesting that they are effective, and arguably such programs have not reached their full potential for curbing childhood or adolescent substance use disorders (Spoth, Greenberg, & Turrissi, 2009).

Critics of psycho-educational programs such as DARE are growing increasingly vocal, challenging the need for and effectiveness of such programs, for a number of reasons. While brief, individualized interventional programs tailored to a student's personality style have been found to be of value (Conrod, Castellanos-Ryan, & Strang, 2010), psycho-educational programs such as DARE use a one-size-fits-all approach that fails to take students' individual needs into account. Further, the question of whether primary intervention for substance use disorders is an educational systems issue has been raised (Zunz, Ferguson, & Senter, 2005). Many school districts find that such programs impose significant demands upon the classroom instructors and detract from already limited classwork instructional time, all apparently with limited benefit to the students. Lilienfeld (2012) even raised the disturbing possibility that psycho-educational programs such as DARE have the potential to harm those who are essentially coerced into participating in the program sessions.

Other critics point out that these programs usually provide negative propaganda about the effects of alcohol or drugs, an approach that has never been demonstrated to work (Leavitt, 2003; Saitz, 2011; Walton, 2002). At best, the critics of psycho-educational programs note that the "evidence suggests that, although knowledge can be increased, and expressed attitudes may be changed, affecting drinking behavior through school programs is a very difficult task" (Room, Babor, & Rehm, 2005, p. 525). An interesting and unexplored potential exception to this analysis is the application of computer technology to psycho-educational intervention programs (Saitz, 2011). This would allow the student to progress through a series

of educational modules at his or her own pace, and, given the growing use of computers by younger age cohorts, will also allow the material to be presented to the learner through a medium they enjoy using. Traditional programs have found that the vast amounts of information provided to the participants will, at best, provide a temporary modification of the individual's behavior (Reyna & Farley, 2006/2007). The application of computer technology to psycho-educational interventions might alter this outcome, although research into this theory is lacking at this time. Newly developed programs such as DARE's Keepin' it REAL (KiR) curriculum attempt to solve some of the criticisms of earlier versions, but much more research is needed before they can be determined to be effective (Caputi & McLellan, 2016).

One very real challenge to psycho-educational programs such as DARE is the ongoing process of marijuana legalization. It is difficult to argue that a compound that is legally sold in your state is a dangerous substance that should be avoided (Suskind, 2016). Further, there is evidence that programs such as DARE are counterproductive, increasing students' curiosity about the drugs of misuse (McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds, 2009). When the child or adolescent experiments with a recreational substance (or knows of a friend who has done so) and they find that the dreaded consequences did not happen to them, the credibility of the information provided is dismissed by the student. A modest body of evidence does suggest that, at least in the short term, programs that use peer interaction and refusal skills training, and that help the student change normative beliefs, are more effective than classroom instructional programs facilitated by a teacher or law enforcement staff member (Windle & Zucker, 2010). Characteristics of such programs include smaller numbers of students (thus facilitating peer interactions), a greater number of contact hours per week, and a focus on social changes outside of the school itself, which were found to be more effective than those programs that focused simply on classroom instruction about the dangers of drug misuse (Windle & Zucker, 2010).

Critics of psycho-educational programs suggest that such programs continue because they give the *illusion* of doing something about the growing problem of childhood and adolescent substance use disorders (Leavitt, 2003; Saitz, 2011). This possibility is supported by the observation made earlier that students are not provided the full continuum of care, and that those students most in need are not served by psycho-educational programs. Fortunately, many school districts are starting to fight back against such programs, citing their lack of proven success and the loss of classroom instruction time as reasons for rejecting such programs.

Reactions to the Bio/ Psycho/Social Model

Although the bio/psycho/social model would appear to be comprehensive in scope when the components are considered together, there are those clinicians who argue that it is the wrong paradigm within which to view psychiatric disorders (including the addictions). Tavakoli (2009) offered five reasons why the bio/psycho/social model is flawed: (1) The bio/psycho/social model further dichotomizes the breach between biological models of the substance use disorders and the psychosocial models of the SUDs. (2) The bio/psycho/social model reinforces the stigma associated with mental illness. (3) Poor behavior is not a “disease,” as is implied by the bio/psycho/social model, as evidenced by the fact that many forms of poor behavior (such as those demonstrated by antisocial personality-disordered persons) cannot be treated by medical science. (4) The term “psychosocial” is poorly defined, leaving the clinician confused about which aspects of the individual’s life are relevant social or psychological factors that must be considered in the formulation of a treatment plan. (5) Finally, the author suggests that the model “antagonizes” (p. 27) medical professionals, who then dismiss possible psychological or social contributions to the individual’s medical status.

In spite of Tavakoli’s (2009) reservations, the bio/psycho/social model has become one of, if *not the* predominant model in the addictions field, and as a whole is rarely challenged (Tavakoli, 2009, being an exception).

Chapter Summary

In spite of almost a century’s effort, no “grand unifying theory” of the addictions has emerged. Some therapeutic theories appear to offer some insight(s) into various behaviors often noted in people who have substance use disorders. However, the degree to which these theoretical models explain the substance use disorders varies from one person to the next. Some who misuse substances appear to use chemicals to cope with psychological distress, while others do so in response to social pressure. Some yield to the pharmacological reward potential of the drugs of misuse, and still others appear to be biologically predisposed to misuse chemicals. In response to this lack of consensus, the American Society of Addiction Medicine has suggested a bio/psycho/social model of the addictions, a model that at this time appears to provide clinicians from multiple disciplines of theoretical support for their efforts to understand and treat the substance use disorders.

The Substance Use Disorders as a Disease of the Human Spirit

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 27.1** Understand the difference between spirituality and religion
- 27.2** Identify the elements that are related to spirituality
- 27.3** Understand how diseases of the spirit can block spiritual growth
- 27.4** Describe the benefits that may come from spirituality

Introduction

Spirituality reflects something of a paradox to society. People often describe themselves as being “spiritual” when they mean to say that they hold strong *religious* values and are active in their place of worship. Paradoxically, one might be active in one’s church without holding strong spiritual beliefs,¹ while a very spiritual person might not be active in any established church. Arguably, this conundrum might reflect the fact that there are no standard definitions for the terms *religion*, *religiosity*, and *spiritual*. The individual’s spiritual beliefs might be said to fall into the “social” part of the bio/psycho/social model of the addictions discussed in the last chapter. Yet the individual’s spiritual beliefs are rarely discussed during bio/psycho/social assessments, in spite of the fact that his or her spiritual belief system is an important part of each person’s identity (Pargament, 2007). This is surprising in light of the fact that the substance use disorders are often said to reflect a spiritual shortcoming within the addicted person. For this reason, this chapter will discuss healthy spirituality as well as what can be considered diseases of the human spirit.

The Individual: The Starting Point

Any discussion of spirituality must begin with the individual. This statement is self-explanatory: Without the individual there can be no spirituality. Humans are spiritual animals, a characteristic that might define *Homo sapiens* as unique among animals on this planet. Even those who disavow

¹A person who is active in their church for social reasons, for example.

spiritual beliefs are, by their very act of denying personal spirituality, acknowledging that it exists: Their denial simply reflects personal choice as to how to relate to their spirituality. For the vast majority of us, spirituality remains an unexplored potential within us that is rarely acknowledged, if not rarely the subject of introspection.

Yet, like other unacknowledged aspects of existence such as gravity, it exists. Medical and mental health professionals rarely discuss the individual's spiritual belief system with their patients. Unfortunately, this is often interpreted as evidence that spirituality is a relatively unimportant aspect of the individual's life, if not an outright denial of spirituality, rather than a lack of training in how to discuss this topic with the individual. One of the exceptions to this rule is when the individual's spiritual beliefs conflict with medical treatment recommendations (Barnes, Plotnikoff, Fox, & Pendleton, 2000; Galanter, 2014).²

Thus, we begin our journey by acknowledging that spirituality exists, although its importance to the individual varies from person to person.

Before Spirituality Is the Individual

Eric Fromm (1968) suggested that we are part of the animal kingdom in the sense that we possess many of the same organs, and the same biochemical processes found in our bodies are also found in the bodies of animals. Children learn early on that humans are mammals and how we fit within the animal kingdom. However, we are also separate from the animal kingdom because we possess a sense of self-awareness (Fromm, 1968). As part of this self-awareness we possess a divine spark of life, a *spirit*, *spiritus*,³ or what some may call life force. This awareness of "self" allows the individual to ask, "What is the meaning of my life?" Another aspect of self-awareness is an imperfect knowledge of our own mortality. This makes us uncomfortable to a greater or lesser degree: Other people might die by accident, disease, or less commonly in combat, murder, or suicide, but these deaths inspire only a vague acknowledgment on our part that at some point in time we will meet a similar fate. The answers to these questions help to establish or maintain our self-image. Finally, within a wide range, we are able to reinvent ourselves.

During the stage play *Man of La Mancha*, the hero, Miguel de Cervantes, is confronted by a cynic for being an author, a dreamer who does not accept life as it is. Cervantes

replies that he has been a soldier, was captured, sold as a slave in Africa, where he labored in the hot sun under the constant threat of being whipped, before escaping to return to his home country. He had held men in his hands as they died, Cervantes said, and they all seemed to be asking the question "why." He did not think they were asking to understand why they were about to die, Cervantes said, but why they had ever been born. So he has seen life without its illusions, he says, and what harm is there in a man living a life that reflects not the reality that exists around him but life as he believes life should be like?

During the process of growth, the spirit is not static: As individuals mature they are guided and shaped through experiences over which they might have little if any control, but to which they can *choose* their response. Immediately upon making one decision, however, the individual discovers that she/he is faced with the need to make another choice (Gawande, 2014). It is for this reason that one could arguably define *spiritus* as the ability to make conscious choices. Surprisingly, these choices both help define the individual and shape his or her growth: "Through repeated interactions that include perceptions of a partner's expectations, individuals can experience shifts—subtle or dramatic—in their attitudes, beliefs, habits and behaviors" (Gawande, 2014, p. 42).

One way that we learn to cope with adverse life circumstances is to take advantage of possible relationships that we encounter as we travel down the road of life. Each of these relationships is an expression of our life force touching (or being touched by) another. We are not obligated to share our life force with another, but retain the power to choose whether to enter into a relationship with another, and how much of our "self" we wish to share. It is also an expression of the person choosing the goals toward which he or she will work (Fromm, 1968).⁴

The individual self also identifies how the person views him- or herself ("self-image") and has the potential to define a *meaning* for his or her life. These are defining characteristics of humans: Within certain limits⁵ we define and set goals for ourselves based upon what we believe is true of ourselves. One important contributor to the individual's sense of identity, or self-image, is the relationships into which the person chooses to enter⁶ (Buber, 1970).

²For example, Sadock, Sadock, and Ruiz (2015) devote approximately one page out of their 1,472-page book *Synopsis of Psychiatry* (11th ed.) to spirituality.

³A Latin word that can refer to *spirit* or *breathing*, both characteristics of life.

⁴The individual who has been given the message that they are a failure throughout their lives might build their life goals upon this belief, for example.

⁵We cannot choose the socioeconomic status of our parents, for example.

⁶Other ways through which the individual's self-image or life force is expressed are their artistic interests, hobbies, entertainment, and vocational interests.

During the experience of life, we find that some relationships are forced upon us⁷ and some are based on the conscious choice of the parties involved.⁸ We base our self-concept in large part upon feedback from those in our relationships, which is why the earliest feedback that we receive has such a strong imprint on us. Later in life, the individual begins to select the relationships that he or she wishes to enter into. These relationships offer an alternative to the earlier familial feedback, and might also motivate the individual to examine his or her self, to make decisions about what he or she believes to be true about his or her self.

One method by which individuals seek to learn more about their self is by entering into a relationship with a mentor, a guide through their entry into adulthood and the early adult years. Other people choose to enter into relationship with something that they view as being greater than the self (Gawande, 2014). It is through this relationship that the individual seeks guidance from and assigns meaning to life greater than an interest in social groups, the opposite sex, jobs, college, and postgraduate plans.

However, for those who embark upon this journey, they will encounter opportunities that foster growth and possibly even transform the spirit. To the disappointment of those who would prefer an easier path, such transformation is an active, often difficult process: The individual must actively seek to understand his or her “self,” choose life’s experiences from which to learn,⁹ and those memories that he or she must confront to allow for spiritual growth.

Spirituality

Lamentably, there is no standard definition of spirituality, making it quite difficult to discuss spirituality, much less assess the subject scientifically. Modern models of spirituality have been influenced by a range of social and historical forces unique to Western culture.¹⁰ These social and historical forces have also contributed to multiple interpretations of spirituality and what it means to be a spiritual person. However, the different interpretations of spirituality in Western culture, combined with those of the Middle East and Asia, share the common goal of a *spiritual awakening*, or the

transformation in the soul. Blinded by the demands of materialism, the majority of the population (if they stop to think about such matters at all) view spirituality as a relic from the past that, in these enlightened times, is no longer necessary. Such materialistic persons have learned to seek inner peace through the possession of material things.¹¹ In spite of society’s emphasis on the ownership of material goods as a way to define the self and gain status in this world, a minority of the population argues that the spirit exists within each of us, and that learning about and coming to terms with our inner self has never been more important than it is now.

Modern Spirituality

Although battered and bruised by the social and historical forces of the past five centuries, at the start of the 21st century the concepts of the *soul*, *spirit*, the divine spark of life, or *spiritus* still remain and form the foundation of modern *spirituality*. There remains no consensus as to the meaning of the term, which is perhaps understandable since modern spirituality rests upon a foundation of Judaism, Christianity, Buddhism, and Islam. To further complicate matters, researchers have used the word spirituality differently in various journal articles and books. There is a consensus that the word denotes a lifelong journey of exploring and transforming the spirit. It is a subjective experience that defies quantification (Galanter, 2014),¹² but which is unmistakable to the individual who has experienced a spiritual awakening. The modern concept of *spirituality* suggests a growth of the spirit, of bringing light to those dark regions of the soul that frighten us or of which we are ashamed, a search for a state of inner peace as the quiet furies of the soul are resolved and put to rest. This last interpretation of spirituality demonstrates the influence of psychoanalysis upon the evolution of the concept of spirituality.

Our spiritual journey is a subjective perspective that is constantly changing as people drift into and out of our lives, educational experiences unfold, and as we progress through the various transitional phases of life. The external universe around us is also in a constant state of change: job promotions, lateral transfers, job terminations, births and deaths both within the family and extending to include close friends, storm damage to our homes, new relationships or the end of cherished relationships, etc. We are constantly called upon to adjust to these life-changing events, and our spirituality can be a source of comfort and a source of resilience in the face

⁷Family members, for example.

⁸We might choose our friends, but they also choose us, a fact that most of us forget until our overtures for a relationship are rejected.

⁹Unfortunately, some people choose not to learn from experience, repeatedly making the same mistake in the hope that they achieve a more desirable outcome.

¹⁰The decision of King Henry VIII of England to break ties with the Catholic Church is one such historical force, for example.

¹¹Wearing the latest clothes, listening to the latest music, driving the most expensive car with the latest options package, etc.

¹²How can you measure the beauty of a sunset, for example?

of adversity. Spiritual transformation helps to shape life decisions, personal identity (or the self-concept), self-knowledge, interpersonal relationships, a source of relaxation or distancing from life's pressures, and perhaps most importantly it helps the individual select a defining purpose in his or her life (Milstein, 2008; Pargament & Sweeney, 2011).

There is no single road or activity to achieving what is referred to as "spirituality." There are also no signposts to measure spiritual growth. It is a *personal* journey: If the individual is progressing in a healthy direction, the spiritual growth will have a positive influence on the individual (DiDonato, 2015). Some of those who have embarked on this spiritual journey believe that it continues after death, although this is not a universal belief. Over time, a large percentage of those who embark on a spiritual journey sense or encounter something or some being to guide them—what can only be described as a metaphysical or "Higher Power"¹³ that becomes the center of their spiritual transformation (Galanter, 2014). By definition, the Higher Power is greater than the individual, and one way the individual then defines the self is how he or she relates to that power.

This is also true in the individual's relationship with his or her Higher Power. Healthy relationships can challenge us to grow and learn about ourselves, while unhealthy relationships hold the potential to do just the opposite. Further, as we mature we gain different perspectives into our insights and beliefs about our self and re-examine our past on the basis of our growing maturity, new insights, and beliefs. To illustrate this process, what was important to us, and what we believed was true of ourselves when we were 16 would probably be far different to us when we were 26, for example. Thus, as we repeatedly interact with our perceived Higher Power, our attitudes, beliefs, habits, and behaviors might change in a more positive (or negative) direction.

An unknown percentage of those who explore their spirituality do so through participation in an organized religion. Participation in an organized religion, however, is not necessarily seen by all as required for spiritual growth. **Religion** itself is an *organized set of beliefs*, which are often described in certain texts considered sacred by believers of the religion. Adherence to the beliefs specific to that religion is thought to provide a framework for spiritual growth (Ameling & Povilonis, 2001; Pargament, 2007).

If the individual is engaged in a personal spiritual journey, several forces will shape the parameters of that voyage

of exploration. The first of these is **faith**. Faith involves the development and expression of confidence in the tools and goals of one's spiritual journey in the face of doubt. If the goal of the individual's spiritual journey is to build a relationship with his or her Higher Power, then faith is expressed through the individual's confidence in that Power in the face of doubt. Doubt helps to define faith: If a Higher Power¹⁴ were to announce its presence in such a way that it could not be doubted, then there would be a need for neither faith nor doubt. It would be like gravity: We would just take it as a given in life and not give it a second thought.

Communication was one of the tools that helped humans conquer this planet (Marean, 2015), and it is an equally important part of the individual's spiritual journey. Although we tend to think of verbal communications (what we hear), communication takes place on multiple levels. The most basic and possibly most powerful means of communication is the power of touch (Denworth, 2015).¹⁵ Eye contact is also a way to communicate emotions as well as social dominance, and, in spite of efforts to the contrary, often reveals attempts at deception. However, true communication is exceptionally difficult: We have all experienced those moments where in the middle of a two-way conversation we suddenly stop and ask, "Wait a moment! What did you just say?" In most conversations we are only half listening to the other at best: We are busy framing our response before the other person has finished talking. It is not uncommon to realize that the other person said something of special interest, which we missed for this reason. It is difficult at first to just sit still and *listen* without speaking, and so we often drown out that little voice "in the back of our heads" that many say is our Higher Power reaching out to us in response to our questions, concerns, frustrations, etc.

Our growing sense of self-awareness during childhood and adolescence brings with it the concurrent growth of *self-determination*. This freedom, however, requires that the individual take *responsibility* for his or her choices (Fromm, 1956, 1968). This ability to choose and to accept responsibility for one's choices is perhaps best illustrated by the actions of martyrs who willingly follow a course of action that they know will result in their deaths (Eberstadt, 2013). Other examples abound: We end a relationship because it does not feel "right," or because we recognize fatal flaws in the relationship and do

¹³The term *Higher Power* is not being used in a religious sense, although many will choose to use the Higher Power specific to their religion. Rather, the term in this text is used in the sense that a Power is greater than the individual, is beyond his or her control, and encourages personal growth.

¹⁴The author prefers the ancient Hebrew term "He-Who-Has-No-Name" for the Higher Power, since by naming a Higher Power we limit its being by forcing *our* definition upon a being who, by definition, is greater than we are.

¹⁵Example: the laying on of hands or anointment with holy oils in certain religions.

not wish for it to progress further. These are examples of self-determination for which we must take responsibility.

Another element of spirituality is one's *commitment*. This is an act by which a promise is fulfilled. A person who borrowed 10 dollars from you with the promise to repay the loan at the end of the week has made a commitment. This is a minor example of what a commitment means. Few people call attention to the fact that they are acting on their spiritual beliefs; however, examples of commitment to one's spiritual beliefs abound. The firefighter who rushes into a burning building to search for persons who might be trapped usually does not stop to announce, "I am doing this because of the dictates of my spiritual beliefs." They are simply doing what firefighters do because their commitment to their calling is so ingrained in their "self" that they do not stop to think about it. In another example, the person who stops you to return your wallet after it has slipped out of your pocket in a convenience store might very well be demonstrating an unconscious commitment to his or her spiritual values. When practiced for a long enough period, our spiritual beliefs and values become an unconscious expression of our self. This is one way that true spirituality provides a sense of being "grounded." It is also through our commitment to our spiritual path, even in the face of the pain that we encounter in life, that we discover deeper layers of our spiritual life than we thought existed when we began our spiritual journey.

Relationships are not static entities but evolve over time. As Gazzaniga noted:

The concept of layering can be applied to almost any complex system, even our social world. One layer functions nicely, driving us with its particular reward systems. Then, suddenly, we can be bumped into another layer where different rules apply.

Gazzaniga (2015b, p. 5)

Commitment also reflects our obligation to maintain a relationship as it moves from layer to layer. This is true of our relationships with other persons as well as with our Higher Power. Examples of this layering effect are found in our daily lives: Our relationship with our parents when we were 3 most certainly is far different than when we were 23, for example. Our relationship with our parents is at a different stage or layer at each of the two ages cited in this example. This is equally true in a marriage: It is virtually impossible for those who have been married for 10–12 years to say that they are exactly the same as when they were when they first married. Each partner provides a challenge and a means for the other to grow as the couple faces the trials and demands of daily life. The demands of parenthood provide additional opportunities for spiritual growth as the parents learn to place the child rather than their selves at the center of their lives. As the infant grows

into childhood and eventually adolescence, the parents must learn to encourage stage-appropriate **individuation**¹⁶ for their child until he or she enters adulthood.

Admittedly, growth in any relationship is painful. As parents of a newborn infant might attest, their bundle of joy quickly begins to assert his or her own wishes and demands. Much to the consternation of the parents, this drive toward independence continues through childhood, into adolescence, and hopefully culminates as the individual becomes a young adult. As much as the parents might wish otherwise, their infant or child does not alter his or her behavior to meet their expectations. The infant's job is to be an infant, and the child's job is to be a child. The parents will find raising their infant to be rewarding, frustrating, and possibly both simultaneously, but they must learn how to adapt their lives and expectations to accommodate this stranger that they have created and brought into their lives, and to prepare him or her to in turn become an adult.

This rule applies in our other relationships: As much as we might wish otherwise, it is not the responsibility of another to live up to our expectations. Through communication and negotiation, the couple might come to agree upon the same goals, such as when the marital partners agree that one will go to school while the other works to support them, for example. However, in committed relationships there will also be disagreements about priorities, child discipline techniques, financial issues, and sexual compatibility, to name just a few of the issues that couples argue about. The commitment that we make in a relationship carries with it the expectation that while couples can (and often do) disagree, this will not become a power struggle between the partners.¹⁷ If this should happen, one or both of the individuals involved probably is demonstrating a degree of false pride (discussed below).

Another aspect of commitment is that of *respect* for the other, or possibly even *reverence* for the Higher Power of the individual's choice. Respect can be demonstrated in many ways, including treating others as you would wish to be treated, and not seeking revenge if another should commit an act that harms your self. *Listening* is interpreted as a sign of respect in many cultures, with the words of the elderly being held in special reverence because they contain wisdom that comes with age. Holding your Higher Power in high regard and speaking to your Higher Power with respect is especially important. *Listening* to your Higher Power is even more important. You are talking to a being that is far greater than

¹⁶ See Glossary.

¹⁷ There are a number of self-help books addressing the issue of conflict resolution in an ongoing relationship available through any bookseller.

yourself, and, if only for that reason, your Higher Power deserves your respect.

An additional sign of respect is demonstrated when the individual demonstrates true *humility*. Humility does not mean hiding our accomplishments from others, nor does it mean groveling before them. Rather, true humility means that we have an honest understanding of who we are at this moment, and thus do not need to prove anything to anybody. *Humility is demonstrated through our behavior.* Two excellent examples are the firefighter who enters a burning building to look for trapped people, or the military medic who braves enemy fire to rescue a wounded soldier. If you were to ask either of these people why they put their lives at risk, they would probably respond with something like, “Well, that’s what I get paid to do,” or “It’s just the right thing to do.” It is quite unlikely that either of these hypothetical people would answer “to impress people.”

Yet another aspect of humility is that we give up the pretense of being entitled to judge others.¹⁸ Gazzaniga (2015a) observed how he was surprised to learn that smart people seem to delight in pointing out how stupid other people seem to be. We do not have the right to judge another for not being as smart as we think they should be.¹⁹

One element of humility is that of *forgiveness*. Forgiveness is frequently misunderstood in this culture. It does not mean that we simply forget about how others have hurt us. It might be interpreted more as a selfish act in which we reclaim the energy that we invested in being angry at another for their past behavior. How often have you heard about how person A carried a grudge against person B for months or even years, only to find out that person B had passed away weeks, months, or years ago? At that point person A might consciously decide that it just is not worth remaining angry with person B any more, since the individual is dead. This hypothetical example illustrates how forgiveness is a process of learning to “let go” of your resentment(s) and reclaiming the emotional energy that you invested at being angry with them. We might maintain vigilance to protect ourselves from the possibility that they, or others, will repeat the behavior that hurt us so deeply. Forgiving another person does not mean that we forget. In forgiveness we choose to let go of the anger and resentment rather than allowing it to continue to harm us.

One frequently overlooked element of a healthy spiritual life is that of creating a **ritual** around one’s spiritual life and

other life activities. This is not to imply that the individual must engage in the elaborate prayer rituals seen in virtually every one of the world’s religions. Rather, the word *ritual* is used here to reflect a uniform time and procedure in each day’s schedule for the individual to sit, reflect upon, and discuss his or her problems with his or her Higher Power. *Quiet is an absolute part of this process.* Some individuals report that having a recording of Gregorian chant²⁰ playing in the background both helps to negate outside sounds that might intrude and provides a focus for the individual’s thoughts. Other individuals find that the use of incense, or turning the lights off to leave the room lit only by a single candle helps them to detach from their day’s stress while they discuss problems with or contemplate their Higher Power. It is essential to include this time for communion (or “common union”) with one’s Higher Power at the same time each day until it becomes a part of your unconscious planning for the day’s activities. Some individuals find that engaging in this quiet time for contemplation right after waking is quite helpful, while others find that engaging in this ritual just before going to bed for the night is a restful way to disengage from the day’s stress. This period of contemplation and communion with your Higher Power need not be time-consuming. At first, the individual’s mind will wander and he or she might find him- or herself preoccupied with day-to-day problems. However, as the individual gains experience meditating with his or her Higher Power, these problems seem less important as one begins to experience a sense of inner peace.

Finally, *honesty* is an important component, perhaps the most important element of our spiritual journey. If we are dishonest with our self and our Higher Power, then what is the purpose of embarking on such a spiritual journey? If we are going to be dishonest with another person, why be in that relationship? There is a difference between dishonesty motivated by unconscious defense mechanisms and intentional **dissimulation**.²¹ Honesty is part of humility: “This is who I am, as I understand myself at the moment.” We might not like what we discover about ourselves when we are honest, but that is part of who we are. Others may enjoy our self, or choose to reject us for a variety of reasons. It is not our responsibility to live up to the expectations of others, but to be ourselves.²² Another person might offer feedback that calls attention to a part of our self that we discover is undesirable to us. We can choose to invest the energy to change that part

¹⁸You are entitled to judge the *behavior* of others, but not the person.

¹⁹Although as often as not the other person’s strengths simply lie in another area. I may have a friend who can make a car do everything but sing, whereas when it comes to automobiles the extent of my knowledge is that it requires gasoline on a regular basis. Different people, different areas of expertise or abilities.

²⁰Which were designed in part to help the individual achieve a contemplative state of mind.

²¹An example of *honesty* is whether you admit to another person to having to look up the meaning of the word or not.

²²The converse is also true: It is not the job of another to live up to our expectations. The job of the other person is to be his or her own self.

of our self, or to disregard the feedback and hold on to that part of our self that we discover is undesirable, but which we fear to confront.

Diseases of the Spirit

Given the details of spirituality outlined above, it is often surprising to learn that there are impediments that might block spiritual growth. You must keep in mind that we are experts at deceiving ourselves. Perhaps the greatest threat to spirituality is the individual's delusion that he or she is sufficiently spiritual and that he or she can discontinue the spiritual journey. By way of analogy, that is like saying that your physical growth is complete when we begin the first day of college. We all know our weight (and its distribution) when we enter college is not necessarily the same as it might be when we graduate from college. Many of us struggle to control our weight, just as many of us will have to struggle to continue on our spiritual journey. Yes, it takes time to continue that journey (just as it takes effort to control your weight), but the results are worth it.

Another expression of this disease of the spirit is our belief that we can follow our spiritual path on "auto pilot." The author of this book was fortunate enough to attend a church service in which two lines on the printed program had accidentally been reversed. Traditionally a single song was sung by the congregation *before* the offering was collected, but on this one week the song was listed on the program as *following* the collection of the offering. Members of the congregation were unsure as to how to proceed and *furious* at the change, probably because now they had to *pay attention* to the service rather than simply follow by rote memory.²³

There are two special conditions that identify spiritual disorders that are not clearly diseases of the spirit. The first is the danger of self-deception in believing that one is "spiritual but not religious." For many, this statement is an apt description of their spirituality. For some, however, it reflects the individual's mistaken belief that he or she is spiritual "enough," though upon close questioning he or she might admit that he or she has not actually engaged in any spiritual contemplation in months or even years. Believing that you are a good person, even if you do behave in an exemplary manner, does not automatically mean that you are "spiritual." Another spiritual disorder is losing one's way on the spiritual path. Asking for guidance from other, more experienced members of the same spiritual community often is sufficient to find the

road back to our spiritual journey. The final condition, which does better approximate a spiritual disease, develops when we focus our energy on the day's inconveniences rather than setting aside a specific time for introspection and spiritual growth each day.

False Pride

We are very good at asking for special favors or dispensations from our chosen Higher Power, but few of us *listen* for the answer. An even smaller percentage of those who ask for such dispensations accept the answer if it conflicts with their wishes. This is perhaps understandable for the parent who fervently desires that his or her Higher Power intervene when their child is very ill. However (and this is where this disease of the spirit overlaps with that of false pride), is it for the individual to believe that his or her Higher Power "owes it to me" to intervene in just the way he or she wants? Such failure to listen combined with false pride makes it difficult to hear another (including our Higher Power) say "no" to our request (Sills, 2013). The Higher Power remains that, a Higher Power: He-Who-Has-No-Name does not *owe* us anything, does not have to grant our every request, and to believe otherwise could be interpreted as a form of false pride.

False pride, or its close cousins *arrogance* and *sense of entitlement*, are the antithesis of humility. False pride usually reflects the prideful one's insecurity, not their achievements. You do not need to prove yourself to others or to whatever Higher Power you select. You just need to be yourself, something that most people seem to feel uncomfortable doing.²⁴ People filled with false pride usually present an image for others to see, but which is only a hollow shell without substance behind it. It is the insecure man who looks for a fight to "prove" that he is a man.

Entitlement is another expression of false pride and is demonstrated when we convince ourselves that we have the right to special treatment: We should be entitled to use the handicapped parking spot because we are in a hurry, there are two other empty handicapped parking spots just a little further away, etc. Few people who believe "I am entitled" seldom stop to ask themselves "Why am I entitled?" We all demonstrate this disease of the spirit to some degree. For example, we have all swapped stories about public figures whose names were in the media for one transgression or another. We rarely talk about how they were exonerated for their earlier reported transgression if this is the outcome of the incident under discussion. We want to talk about the "dirt" on

²³This, by the way, is an excellent example of an *inconvenience* and not a problem. Not a single member of that congregation died because they were now forced to pay attention to the rest of the service.

²⁴Just for fun, the next time you go to a party, listen to how often people introduce themselves, then go one to explain what they do. For example: "Hi, I'm John. I teach science at [fill in the name of your favorite school here]."

another person, not about how the dirt failed to stick when they were found to be innocent. Another reflection of false pride is the belief that we have the right to maintain a grudge against another person. “I am entitled to be angry with X because they did such and such.” *The right to judge another person is an illusion* that draws us away from our spiritual path. That such thinking is an illusion is demonstrated by the fact that we believe we should be forgiven for the times that we have hurt others because our motives were pure, or that our treatment of the other was justified for some reason. We are all flawed and we all do or say things that we later wish that we could take back. We might judge the *behavior* of another person, but not the person themselves.²⁵

The *spirituality of convenience* is a special disease of the spirit. A spirituality of convenience is like a light switch: We turn our spirituality on when it is to our advantage to do so and off when our spiritual values are inconvenient. Imagine, if you will, a person (whom we will call A) whose spiritual beliefs prohibit sex outside of a committed relationship. While away from home for a week-long business seminar, this individual discovers that he or she is attracted to a very desirable partner (person B) who is also attending the business seminar. Person B seems to reciprocate the feelings. The question is: Does A continue to follow his or her spiritual values or take advantage of the opportunity for a brief sexual liaison? Following a spiritual path involves a commitment to follow a certain code of conduct in spite of temptations. Yet how often do we allow ourselves to stray from our spiritual path for our own purposes? It is just a minor deviation from our spiritual beliefs, we rationalize to ourselves, or we will simply do penance after confessing our transgression.

Failure to Maintain a Commitment to Your Spiritual Beliefs

Spirituality involves a lifelong journey of exploration of the self and our relationship with a Higher Power. The failure to maintain a commitment to one's spiritual beliefs might, by analogy, be compared to being on a diet. When we diet, we all “slip” from time to time. How we respond to the slip determines whether it was an honest mistake on our part that we resolve by recommitting ourselves to the diet, or a sign that we have no desire to remain on the diet and return to our former eating habits. This is, admittedly, an analogy, and arguments based on analogies are often misinterpreted.

The failure to maintain a commitment to one's spiritual beliefs might express itself in a number of ways. Failing to

maintain a dedicated time of communion with one's Higher Power is quite common, and people who experience this disease of the spirit often speak of a gradual process through which setting aside time for communion with one's Higher Power seems less and less important as their daily troubles demand more of their time. Unfortunately, this gradual slip from the individual's spiritual path might reflect the possibility that the spiritual path, as one is currently doing things, fails to challenge continued growth. To correct this, the individual must examine the impediments to spiritual growth and take appropriate steps to correct these problems.

Punishment

This spiritual disease might express itself in one of two ways: (a) We may fall into the trap of believing that we can punish our Higher Power. Thus, many people make the threat that if the special dispensation that we demanded (*not requested*) is not granted to us, we then will turn away from the Higher Power. Picture a young child screaming, “If you don't do what I want I will hold my breath until I turn blue” and you will understand this line of reasoning. If we are the one who can punish our Higher Power, who then is the Higher Power? This spiritual shortcoming overlaps with false pride.

A second, unrelated manifestation is (b) the belief that one's Higher Power is punishing us when we (or someone close to us) experiences a serious and possibly life-threatening event. How could our Higher Power do such a thing to us (or the person that we care about)? This is when we must draw upon our *faith* that our Higher Power has a purpose for the actions, even if we do not understand it at the time. We will experience deep doubts about the validity of this statement, but faith and *commitment* will see us through that trial.

Pseudo-Spirituality

This is similar to a *spirituality of convenience*; however, it also might be viewed as reflecting *false pride*, or a lack of *humility* in attempting to threaten the Higher Power. If the Higher Power were so easily swayed by such threats, one would be forced to ask whether it is truly a Higher Power or a target of convenience selected by the individual to ensure that he or she is not challenged to engage in real spiritual growth. Another form of pseudo-spirituality is often seen in cases of “jailhouse religion.” This condition reflects the claim that one has “seen the light,” realized the error of their ways, and reformed. Abusive partners often resort to this line of thinking. Occasionally the individual does discover a road to spirituality, often through participation in a religion of his or her choice. However, in far too many cases, once the individual is released from jail or prison, or their partner agrees to take

²⁵ In criminal court proceedings we are called upon to judge the person's behavior, and punishment is then decided by the court on the basis of their past behavior and the seriousness of the offense.

them back, the spiritual awakening becomes a dim memory as the individual returns to his or her former ways. Unfortunately, it can be extremely difficult, if not impossible, to differentiate between true conversions and those who use spirituality as a way to manipulate others. But their behavior will usually reveal the truth.

Denial of Responsibility

Denial of responsibility is, as discussed earlier in this chapter, the antithesis of responsibility, which unfortunately is rampant in this society. We all suffer from this spiritual flaw to some degree. A popular expression of the denial of responsibility is the use of *blame*. Politicians who are discovered committing some form of transgression are famous for engaging in denial of responsibility: “I am not responsible for [fill in the blank with your favorite transgression]” because (a) “I was intoxicated,” (b) “Everybody else is doing it but I am the only one to be caught,” (c) “I really love my wife and children, who stand behind me as we try to put this unfortunate episode behind us,” (d) “Aliens abducted me and made me do it against my will,”²⁶ or, as more compulsive behaviors are reclassified as addictions, (e) “I have an addiction to [sex, gambling, drinking, etc., etc.] and will be going into treatment for it tomorrow.” A variation of the last excuse is often delivered through a spokesperson, leaving the audience with the impression that the offender has already entered the treatment program.

Some forms of denial of responsibility offered by those who have chosen to commit criminal activity include: (a) “She should not have left such an expensive car parked where it could be so easily stolen,” (b) “I don’t remember that incident because I was drunk [or under the influence of a number of other compounds],”²⁷ (c) “They just left the money there in the cash register and I just could not help myself,” etc. Alcohol does not make the person drink, nor does money make the person steal it: These are behavioral decisions made by the individual. Admittedly, an addictive disorder might make it difficult to avoid following the same road as before, resulting in the same mistakes, but this points to the importance of considering spirituality with those struggling with addictive behaviors or SUDs.

Open Dishonesty

Open dishonesty is the antithesis of honesty. We all are dishonest from time to time: Those little white lies that we think enable us to function on a day-to-day basis in society do count as a form of dishonesty. It is surprising how often we find that we have deluded ourselves about our ability to deceive others, only to find out that they knew about that part of our self already. It often comes as a shock to discover that when we think we have successfully deceived others, we have only deceived our self. The psychological defenses of denial and rationalization often reflect unconscious efforts at spiritual dishonesty that the individual calls upon to avoid facing unsavory aspects of the self.

However, open dishonesty is also demonstrated by some individuals who wish to actively manipulate others into doing their will. This dishonesty, combined with a failure to develop a true sense of humility and a spirituality of convenience, leave the individual vulnerable to developing a distorted sense of importance. Unfortunately, “pandering to delusions of self-importance weakens the true self, and diminishes our ability to distinguish desires from needs” (Norris, 1996, pp. 14–15). Further, if, as Martin Buber (1970) suggested, we define our “self” by our relationships and the manner in which we approach them, then by attempting deception we are in effect defining our self as unreliable and untrustworthy. Extreme dishonesty is one of the legs on which **Machiavellian**²⁸ behavior (Wilson, 2015) rests and might even make up part of the foundation for the antisocial personality disorder.

As the reader should have noticed by now, the elements of your relationship with the Higher Power of your choice share many characteristics with a healthy human relationship. You may also struggle with diseases of the spirit to some degree, but you may realize that the move toward health is the direction desired. This is natural: A relationship with a Higher Power is still a dynamic, evolving relationship that is similar to but perhaps more intense than interpersonal relationships. The qualities outlined above are ideals, not accomplishments. *Nobody* is completely humble, for example, nor can we be entirely aware of our “self.” However, through selective communications with those in our environment we might be made aware of our shortcomings so that we might choose whether or not to work toward resolving these problems.

Thus, at the center of spirituality is the individual and his or her relationships with those around him or her—the individual’s social universe, for want of a better term. Whether this social universe involves a Higher Power, the

²⁶ Admittedly, this author has not heard a politician make this claim, but does believe that it is only a matter of time.

²⁷ Some states actually allow a defendant to make this claim if they were found to indeed have been under the influence of chemicals at the time of the offense, on the grounds that the chemical use resulted in a “diminished capacity” for decision making.

²⁸ See Glossary.

individual's perception of this Higher Power, the individual's commitment toward maintaining a relationship with this Higher Power, and the conditions under which they will work toward maintaining that relationship with their Higher Power are all individual choices.

The individual whose spirit comes to be diseased does not begin life with a damaged spirit. But for some, the accumulated insults over a lifetime come to distort their inner world, and some turn to chemicals to fill the perceived void within, or to ease their pain. Some believe that they are entitled to the chemically induced pleasure(s) of substances, while others find some measure of peace in the arms of a chemical lover that will ultimately betray them in the harsh form of an addiction. This is not unique to those who have an SUD: We all face moments of supreme disappointment (Fromm, 1968). It is at this point in the individual's life that s/he is faced with the choice of either reducing his/her demands to that which is attainable, or turning away from the harsh light of reality to the perceived safety of the chemical's embrace. This is the moment that existential therapists speak of as the time when the individual realizes the utter futility of existence, or of personal powerlessness. At this moment, the individual might either accept his/her place in the universe, or continue to distort his/her perception(s) to maintain the illusion of self-importance through the continued use of chemicals. Spiritual growth involves acceptance of the pain and suffering that life might have to offer, a task that many turn away from. Some become grandiose, or demonstrate the pathological narcissism so often found in persons with an addiction (Nace, 2005a, 2005b).

As long as the individual remembers that this special relationship is not between equals, for in a relationship between equals there can be no Higher Power, then the sense of powerlessness can be freeing. If you have an *open* and *honest* relationship with your Higher Power, you would be open to such feedback about yourself, opening the possibility for change. Such an open and honest relationship does not, as some assert, rest upon a foundation of substance use. It is a voyage of self-discovery that, if successful, allows the individual to learn about the self without such artificial means.

This is the essence of spirituality: It is the expression of a belief in a Higher Power in the face of doubts fueled, in part, by the illusions offered by science. This does not discount the contributions that science has made to our lives. However, spirituality, like many other feelings,²⁹ is not measurable: As part of the individual's spiritual journey, he or she must make a decision whether to enter into a relationship

with that perceived Power. This commitment is then renewed every day: It is not a one-time decision, but, like all relationships, is renewed and evolves each day. This makes sense: I am not the person I was yesterday; I am slightly different from the person I will be tomorrow.

However—and this is a point of confusion in the study of spirituality—it is a *relationship*, which means that it involves *two-way communication*.³⁰ This means that the individual both speaks and listens to the feedback that he or she receives from his or her Higher Power. This feedback is offered in a number of ways: Sometimes it will be recognized in the way the universe unfolds around us, such as when a potential dating partner announces that he or she is moving to a city far away to attend college, or that they are dropping out of school to work. Most often the feedback is reported by the individual as a little voice in the back of their head.³¹ At first that little voice might be lost in the noise of day-to-day living, but as the individual learns when and how to listen, suddenly they begin to recognize when that Higher Power is reaching out to them.³²

Honesty

As was stated above, honesty both with our self and with our Higher Power is perhaps the most important part of our spiritual journey. The opposite of honesty is *dishonesty*, with all that suggests for our relationships with ourselves and others.

Being in a relationship also means a commitment to maintaining that relationship, even if the feedback is not what we hoped for. A marriage is a good example: Imagine a marriage ceremony in which one partner says, "I promise to love and be faithful, except on the first Tuesday of every month."³³ Further, being in a relationship means that you have the *humility to listen*, a trait that few of us are born with and THAT we must struggle to achieve. Most marriage

²⁹Imagine a world where love could be scientifically measured: "It will never work, I'm only 8.5% in love with him/her."

³⁰A one-way avenue of communication is called a *lecture*, such as the one that parents give to wayward children, or the one that you are forced to sit through while in class.

³¹A situation we have all both experienced personally and heard a friend say was that "little voice in the back of my head that kept telling me that I should not do it, but. . . ." Was that "little voice in the back of my head" common sense (not that common sense is very common; if it were, most of us would not get into the trouble that we manage to experience in life), the person's Higher Power speaking to them, or the Higher Power speaking to them *through* what should have been their common sense?

³²A possible example is of a person struggling with their desire to have a drink who fortuitously receives an unexpected telephone call from a friend or parent, distracting them from their internal struggle about whether to take that first drink or not. To be honest, it could also be argued that this was just a coincidence, but there can be no definitive answer.

³³Such a "commitment" does not sound like a commitment at all, does it?

counselors will attest to the fact that few people *listen* to their partner. We spend the time when our partner is speaking planning our reply to the other person's last comment. Being in a relationship means that you are willing to set the self aside for a few moments to listen without bias or preconception to what the other is saying.

History of Abuse

A history of past physical, emotional, or sexual abuse, especially by those to whom the individual normally would turn for comfort and guidance, is not in itself a disease of the spirit. However, the *denial of the self* often seen in those who have been victims, especially when the individual places the needs and desires of others ahead of his or her own, is arguably a spiritual disease. The individual might come to expect additional pain and rejection should they chance to enter into any relationship. In some cases, they are angry because a Higher Power did not intervene when they were being abused or were in pain (Maté, 2010). Admittedly, many who were exposed to such abuse rise above it, but many turn to drugs or alcohol to numb their pain and fill the emotional void left by a lack of supportive, loving relationships (Hari, 2015). If, as Siegel (2008) suggested, relationships shape and direct energy flow both between and within individuals, the individual's history of abuse will help shape and direct this energy flow into the part of the ego that defines the self. They often denigrate themselves and fear a Higher Power because those who have held power over them earlier in life used that power to hurt them.

The Benefits of Spirituality

Even in the 21st century there are many misconceptions about spirituality. The first of these is that we struggle to attain the attributes outlined above. Some propose that we "all start out with hope, faith and fortitude" (Fromm, 1968, p. 20). However, society is frequently not nurturing, and these and other positive attributes over time are stripped away from us. In reality, spirituality is a process of *regaining* these positive attributes that were lost as we matured. This is achieved through the process of spiritual transformation discussed throughout this chapter: We are working to take our spirit as it has evolved over the years, healing the emotional and spiritual damage that we have suffered, and striving to regain the hope, faith, and fortitude that Fromm (1968) referenced. As we mature, we build upon this foundation to add the ability to choose, take responsibility, grow emotionally, be honest with both ourselves and each other, and share all of these attributes with others.

Spirituality is not a waste of time: People who follow a spiritual way of life gain untold benefits from faithfully following this path. Perhaps the foremost of these benefits is a sense of inner peace. The spiritual person gains a new perspective on his or her "problems." Often, they find that unresolved conflict can wreak havoc on our body's immune system from the continual exposure to stress hormones meant to be unleashed for short-term use in crisis situations (van der Kolk, 2014). The spiritual person learns to put problems into perspective and let go of those parts of the problems that are not his or hers to carry.

At this point we must briefly turn aside from the topic of spirituality to clarify the difference between an "inconvenience" and a "problem." The author of this text defines a "problem" as a situation where a person's life is at risk. Anything short of this is an "inconvenience." Now, inconveniences can range from minor to major issues. However, they are still just inconveniences. Imagine two scenarios. Scenario number one: If the airplane on which you are a passenger is about to crash you are facing a problem. In contrast, consider scenario number two: The departure of that plane has been delayed 3 hours because of mechanical problems, causing you to miss an important business meeting. This is an inconvenience; it is perhaps a major inconvenience, but it is still an inconvenience. Nobody's life is at risk in this scenario. Indeed, if the departure is delayed for mechanical reasons, this inconvenience might be saving lives.

With growing spirituality, individuals learn the above distinction, and they also learn to address those portions of issues that they can change and to accept that, no matter how much we might wish otherwise, there are situations where we have little or no control. In the scenario two discussed above, those waiting have no control over the speed with which the plane is repaired: It will take 3 hours. If you walk over to the ticket counter and start to yell, the repairs will still take 3 hours. If you sit back and accept that you have no control over the situation, it will take 3 hours for the repairs to be completed. However, in the time that you are waiting you might read one or two magazine articles, perhaps finish a book you were reading, or use your laptop computer (or smartphone, etc.) to answer messages, etc.

If the individual has a spirituality centered life, then he or she will:

begin to build their lives around the sacred [and] the sacred can begin to lend greater coherence to disparate thoughts, feelings, actions and goals by superseding all other values, integrating competing aspirations into a unified life plan, and [providing] direction and guidance from day to day.

Pargament (2007, p. 72)

Further, many spiritual people report that the inconveniences they encounter seem less important when they turn such issues over to their Higher Power, and that they are less likely to overreact to inconveniences. Again, with growing spirituality, individuals learn to accept and change those portions of situations that they are responsible for and to cease obsessing about the issues they are unable to alter. As the individual learns to become more accepting of issues beyond his or her control, she or he gains an inner peace. They develop a sense of inner peace, and life takes on a new meaning (Galanter, 2014). Physiologically, their bodies produce lower levels of the various stress hormones that cause physical organ damage, which is an added benefit of spirituality (Galanter, 2014).

Further, with growing spirituality the individual learns that when they give up the illusion of being entitled to judge others, they cease to carry the useless burden of anger and hatred that has been part of their lives for so long. What the other person did might have been cruel; however, no matter how angry we might become with another, it will not change their past behaviors. Of course, the individual might be held accountable for their behavior by the society in which they live, and we have the right to detest their behavior. Spiritual persons who belong to a spiritual community might find solace in being able to draw upon the wisdom and strength of others who might possibly reach out to us when we feel most isolated because of our pain. Other members of the spiritual community might have experienced adverse life experiences similar to those we are facing and might help us find a way to come to terms with the adversity we have encountered in life.

Many of those who engage in guided meditation exercises find that they have greater control over their bodily functions than they had thought was possible. Some people report that with guided meditation or biofeedback therapy, their blood pressure has returned to the normal range without the need for antihypertensive medications. Weight loss in the truly spiritual person becomes less of a problem, and in many cases the spiritual person *willingly* begins to exercise and eat a healthier diet. As part of the sense of inner peace that is often achieved through a spiritual life, the individual might find that unhealthy habits such as cigarette smoking³⁴ or excessive alcohol use become unimportant and thus easily renounced. However, the greatest gift of a spiritual life is that of *inner peace*. This peace is achieved through the transformation of the soul, not forced

on the self through chemicals (either prescribed or as drugs of misuse).

There is a growing body of research into whether spiritual people live longer than those who do not identify as spiritual, and whether this longevity is healthier as well (Zimmer et al., 2016), despite the previous lack of research related to spirituality and the relation to mental health (Walsh, 2011). There is clear evidence that spirituality and positive mental health outcomes are linked, although further development of theory in this area is called for (Levin, Chatters, & Taylor, 2011). Individuals who have a greater sense of purpose and meaning in life tend to have increased sensitivity and empathy toward others (Giordano, Prosek, & Lankford, 2014). They report a greater awareness of and willingness to respect interpersonal boundaries, and they become more confident when saying “no” (Sills, 2013). They also learn how to accept having another say “no” without it shattering their self-esteem (Sills, 2013). As the information briefly reviewed above suggests, there are very real benefits to an active spiritual life, although these benefits are often subtle and remain hidden from nonspiritual individuals for the most part. Although therapy as we know it today began within religious and spiritual circles, it shifted toward the secular and nonspiritual for some time (Wampold & Imel, 2015). As evidenced by the growing interest in spirituality and the increasing body of research, future research is anticipated to provide further support for an active spiritual life.

The Addictions as a Disease of the Spirit

As will be discussed in more detail in Chapter 35, there are many who view the substance use disorders as a disease of the spirit, at least in part. From this perspective, the person who misuses substances might be viewed as being on a

spiritual search. They really are looking for something akin to the great hereafter, and they flirt with death to find it. Misguided, romantic, foolish, needful, they think that they can escape from the world by artificial means. And they shoot, snort, drink, pop or smoke those means as they have to leave their pain and find their refuge. At first it works. But, then it doesn't.

Baber (1998, p. 29)

In short, those who misuse substances are viewed by adherents of the spiritual model as attempting to gain the benefits of spirituality without the long journey necessary to achieve the peaceful sense of unity with the universe and the Higher Power of their choice.

³⁴ In Chapter 16, we discussed how many smokers use the rituals of cigarette smoking as a way to cope with stress, which with growing spirituality becomes less of a problem for the individual.

Chapter Summary

The concept of spirituality has been debated for centuries, both among adherents of one spiritual community and between different philosophical schools of thought. Currently, spirituality is perhaps best envisioned as a subjective process through which the soul is transformed to become a vessel of inner peace, inner bliss, or freedom from the mundane demands of daily living. There are many paths that people use to develop spirituality, including the practice of yoga, meditation as practiced by the Buddhist or Shinto religions, and a

wide range of other religious traditions. While participation in an established religion is not necessary for the individual to become spiritual, some individuals find that the guidelines and rituals of their chosen religion are an essential part of their spiritual journey. Along the way many, perhaps most, people encounter what they call a Higher Power, which they define in a variety of ways depending upon their individual perception of this Being. With this discovery, the goal of the spiritual journey often becomes the union of the “self” with this Power to achieve the inner peace sought by the spiritual person.



CHAPTER 28

The Assessment of Suspected Substance Use Disorders¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

28.1 Understand the theory behind substance use assessments

28.2 Distinguish between screening for and assessment of substance use disorders

28.3 Review various ways to screen for substance use disorders

28.4 Review various ways to assess substance use disorders

28.5 Describe a potential format for writing an assessment report

28.6 Understand the purpose of diagnosis

[The] successful treatment of substance use disorders depends on a careful, accurate, assessment and diagnosis.

—Greenfield and Hennessy (2008, p. 55)

Introduction

As Samuel Shem (1978) wrote in his novel *The House of God*, “If you don’t take a temperature, you can’t find a fever” (p. 420). This dictum applies to substance use disorders as well: Many health care professionals avoid discussing the patient’s substance use or misuse to avoid having to deal with this uncomfortable topic. This might be why the majority of referrals to substance rehabilitation programs do *not* come from health care providers (Madras, 2010). Few future doctors receive training in screening and assessment for substance use disorders during their family medicine rotation (Carlin-Menter, Malouin, WinklerPrins, Danzo, & Blondell, 2016). Unfortunately, there is a consequence to this therapeutic myopia: The substance use disorders (SUDs) are all too often an unacknowledged causal factor in various disease states, in addition to their contribution to the problems experienced by clients with co-occurring disorders,² not to mention the various legal, financial, interpersonal, vocational, and personal problems caused, or at least exacerbated,

¹The assessment of suspected child or adolescent substance use disorders, and instruments used for this purpose, is discussed in Chapter 20.

²Discussed in Chapter 25.

by SUDs. These problems make it imperative that the health care professional obtain an accurate history of the patient's substance use patterns (Johnson, 2003). Further, in this era of the ever-changing health care insurance system in this country, where the health care professional must obtain "prior authorization" and justify each procedure in advance to ensure maximum return for each dollar spent on health care, the need for a referral to rehabilitation must be firmly established on a bedrock of clinical data.

This foundation is established, in large part, through the process of assessment. This process serves the dual roles of (a) helping to identify those individuals who require professional assistance to help them come to terms with their substance use disorder; (b) serve as a "gatekeeper," providing justification for admission to the proper level of treatment and identification of strengths and weaknesses on the part of the individual; and (c) form the foundation of the rehabilitation process (Juhnke, 2002). In this chapter, the process of assessing an adult with a substance use disorder, and how the assessment process relates to the process of rehabilitation, will be explored.

The Theory Behind Substance Use Assessments

It is not uncommon for inexperienced health care professionals to cite evidence of a single episode of illicit drug use, or a positive urine toxicology test,³ as *proof* that the individual is addicted to chemicals (Washton & Zweben, 2006; Winters & Kaminer, 2008). In reality, the use of a substance, even if that substance is illegal, does not prove that the individual has an SUD (Gitlow, 2007). These facts simply underscore the need for a complete substance use assessment to determine whether a given individual has an SUD. This assessment process is "more than a one-time paperwork procedure conducted at the onset of treatment to simply gather minimal facts and secure a . . . diagnosis" (Juhnke, 2002, p. vii). It is the *first step* in the rehabilitation process (if rehabilitation is necessary), and it continues throughout treatment as the individual's needs and resources are continuously assessed and addressed (Daley & Marlatt, 2006; Donovan, 2005).

Life would be much easier if there were a Holy Grail for the detection of SUDs (Fleming, Mihic, & Harris, 2001, p. 321). That such an assessment process will emerge in the

near future is unlikely, as scientists have yet to agree upon a standard definition of even the basic term *addiction* (Erllich, 2001; Fletcher, 2013). Thus, the assessor must go into the assessment process with imperfect tools, and then is asked to make a diagnosis that might have lifelong implications for the patient. One hypothetical example might be the individual's ability to purchase affordable health care insurance at the age of 50 after a diagnosis of an SUD made when s/he was only 20 years of age.

The assessment process is complicated, and involves several steps. The process of **screening** a patient is carried out to identify those patients who *might* have a certain disease or condition (Knight, 2005). It is not about simply testing, but instead is aimed at determining what next steps may need to be taken, including whether further assessment is needed (Morgen, 2016). If all individuals who misuse substances were alike, then there would be no need for the assessment process to move beyond the determination of whether the individual does or does not have a chemical use problem. However, all those who misuse substances are not the same, and there is no one-size-fits-all presentation of substance use. Clients vary as to their age, gender, marital status, culture, ethnicity, degree of insight into their problem(s), legal status, medical condition, mental health condition, and willingness to change (Greenfield & Hennessy, 2014). Thus, the clinician must consider a wide range of factors during the screening process, and if there is reason to suspect a substance use disorder is present, a complete **assessment** should then be carried out. This is done to confirm or rule out the presence of that disorder, assess its severity, identify individual strengths, and help guide treatment (Blume, 2005; Knight, 2005). It is at this point that the assessment process enters its final phase: that of *diagnosis*. Each of these interrelated steps will be discussed in more detail below.

Screening

The core of the screening process is the *clinical interview* with the client (Greenfield & Hennessy, 2014). The clinical interview must be long enough to allow for the assessor to build a complete overview of the client's substance use patterns (Greenfield & Hennessy, 2014). Screening should not be limited to just one substance (Morgen, 2015). Greenfield and Hennessy (2014) suggested that gathering information be done through a number of avenues: the client's responses during the clinical interview, collateral information, standardized questionnaires, a review of past records, and biological testing. While questionnaires and biological testing information are valuable to the assessor, *a test score or result by itself does not establish whether the individual does or does not have*

³Which is to say a urine toxicology test that reveals evidence of illicit drug use.

an SUD! The test score is but one perspective on the individual's substance use pattern.

"Screening is aimed at detecting the entire spectrum of unhealthy use, from risky use, to use with problems, to a diagnosable disorder" (Saitz, 2015, p. 100). Screening does allow for early intervention for those who may be at risk of developing an SUD, but also to identify those who do currently meet criteria for an SUD (Saitz, 2015). Screening is conducted when we do not know if a particular individual has the symptoms of an SUD (Saitz, 2015). If we already know that a person has an SUD, then the next step is assessment, which would then lead to treatment recommendations (Saitz, 2015). Morgen (2015) stressed the importance of screening going beyond just substance use disorder treatment programs, but moving into primary care settings, emergency rooms, and college counseling settings, to name a few.

Verbal Screening Aids

A popular screening instrument used for quite some time is the "CAGE" questionnaire (Mayfield, McLeod, & Hall, 1974). It was popularized further by Ewing (1984). CAGE is an acronym for the four questions used in this screening tool:

- Have you ever felt that you should *cut down* on your drinking?
- Have people ever *annoyed* you by being critical of your drinking?
- Have you ever felt bad or *guilty* about your drinking?
- Have you ever needed to have a drink the first thing in the morning to steady your nerves, or get rid of a hangover (*eye-opener*)?

It was suggested that a "yes" response to one question suggested a need for a more thorough inquiry by the assessor, while "yes" responses to two or more items suggest that the individual has an alcohol use disorder. Unfortunately, the CAGE questionnaire has been found to have serious problems: First, the CAGE is limited to possible alcohol use disorders (Saitz, 2015). The CAGE-AID was developed to screen beyond alcohol use, while still considering alcohol use at the same time (Brown & Rounds, 1995). These measures are not sensitive to binge activity, nor do they identify the individual's level of consumption (Cooney, Kadden, & Steinberg, 2005). Further, they are not time-sensitive in the sense that persons who have a history of misusing alcohol or drugs but who are currently abstinent are identified as having a problem because of their history (Cooney et al., 2005). Further, both are very vulnerable to deception (Stein & Rogers, 2008). Finally, the CAGE has been shown to be of limited value as a screening instrument for adolescents (Knight, 2005), women, and minority members who have an alcohol

use disorder ("Screening for alcohol problems—an update," 2002), or for persons in the earlier stages of an alcohol use disorder (Washton & Zweben, 2006). Because of these (and possibly other, yet to be identified) flaws, the CAGE is estimated to miss up to 50% of at-risk drinkers (Fleming, 1997).

Another early screening tool is the Michigan Alcoholism Screening Test (MAST) (Selzer, 1971). The MAST is composed of 24 questions asked during a clinical interview that can be answered either "yes" or "no" by the respondent. Scores are weighted with a value of one, two, or, in some cases, five points (Craig, 2004). A score of seven or more points is interpreted as evidence that the individual has an alcohol use disorder (Craig, 2004). While the MAST is a popular screening method still utilized by many, it does present some inherent problems. First, it does not properly identify the full spectrum of misuse, as it is more fitting with severe SUDs (Saitz, 2015; Vanable, King, & deWit, 2000). Second, it provides only a crude measure of the individual's possible alcohol use problem. Third, the intent of the items on the MAST is readily apparent, and thus subject to dissimulation if the test taker should be less than honest (Stein & Rogers, 2008). Next, it is insensitive to binge drinking, and it does not address the use of compounds other than alcohol. Finally, it does not differentiate between the individual's current and past drinking history, the result being that abstinent drinkers could be identified as having an ongoing alcohol use disorder on the basis of their response set (Schorling & Buchsbaum, 1997). Thus, the MAST is best suited to the detection of individuals with a severe alcohol use disorder, and should be interpreted with caution. Some recommend that it not be used at all for screening (Saitz, 2015).

To address the problems with the early screening questions' focus on alcohol use, the team of Brown, Leonard, Saunders, and Papasoulioutis (1997) suggested a simple, two-question screening, which they called the two-item conjoint screening (TICS):

1. In the last year, have you ever drunk or used drugs more than you meant to?
2. Have you felt that you wanted or needed to cut down on your drinking or drug use in the last year?

The authors suggested that, in spite of its brevity, the questions can help to screen, identifying more than 80% of those who had a diagnosis of an SUD. However, this instrument also can yield false positive results, warned the authors, and so one should not rely too heavily on this (or other) verbal interview responses to rule out an SUD, but should consider the responses as one piece of information to be used in the screening for SUDs.

Another rapidly administered verbal tool is the TWEAK (Chan, Pristach, Welte, & Russell, 1993). The letters serve

as a useful mnemonic device for the assessor to remember to ask the client whether they have developed (a) tolerance to alcohol or drugs, whether or not others have ever been (2) worried about their substance use, whether the client has ever used an (3) eye-opener in the morning, (4) had amnesia (blackouts) during periods of substance use, or (5) made attempts to cut (K) down on substance use (Johnson, 2003). A negative answer to all of these questions does not rule out an SUD, but does suggest that the patient probably is at low risk for such a problem. Alternatively, a “yes” answer to one or more of these items suggests a possible SUD.

The team of Smith, Schmidt, Allensworth-Davies, and Saitz (2010) suggested that a single question was able to identify a person with a drug use problem 100% of the time. The question was simply: “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?” However, this question is also rather obvious in its intent, and thus vulnerable to dissimulation should the individual be predisposed to hiding one’s misuse.

Paper-and-Pencil/Computerized Screening Instruments

Self-report instruments offer the advantages of being inexpensive and that they may be less threatening to the client than face-to-face interviews since clients might experience feelings of shame, distrust, hopelessness, and discomfort during the face-to-face interview (Greenfield & Hennessy, 2008). Many of the verbal screening methods addressed above are often administered in paper-and-pencil format and also in computerized format, at times due to the challenge for the clinician of memorizing the questions for lengthy screening measures (Saitz, 2015). A disadvantage of self-report instruments is that they are more vulnerable to client attempts at deception, and are designed with the assumption that the client is reasonably literate. Additionally, keep in mind that such instruments do not *prove* that a person has a substance use disorder (Washton & Zweben, 2006). However, when used properly, such instruments provide the assessor with an additional source of data that could either screen out those who do not have an SUD, or could be incorporated into the assessment process for those who do.

One way to minimize the danger of deception is to administer different instruments that cover the same aspect of the client’s behavior. A client who denies having alcohol-related blackouts on one instrument but who admits to having blackouts on another instrument has presented contradictory information. In such cases, the clinician should attempt to reconcile the two answers by discussing the discrepancy with the client. Another technique is for the same instrument

to be administered at different times, perhaps a week apart, for example, and then the client’s responses are compared. Again, there might be significant discrepancies between the two response sets, which should be explored by the clinician.

Sometimes the client will consent to having his or her significant other sit in the office while the clinician reviews the results with the client. If the client has answered a test item on the Michigan Alcoholism Screening Test addressing alcohol-related motor vehicle accidents negatively, the significant other might then ask, “What about that time when you drove your car into a ditch two years ago?” In this hypothetical example, the client might respond that the police had ruled the accident was a result of ice-covered roads, but then his or her significant other might then go on to say, “But you told me that you had been drinking earlier that night!” The clinician must then determine to the best degree possible whether that person’s alcohol use was a factor in the accident.

A screening instrument developed by the World Health Organization (WHO) is the Alcohol Use Disorders Identification Test (AUDIT). The AUDIT was standardized on samples drawn from six different countries around the world, with the intent of developing a short, easily administered screening instrument that might be used in different countries for the identification of persons in the early stages of developing an alcohol use disorder (Babor, Higgins-Bridle, Saunders, & Monterio, 2001). The AUDIT is composed of 10 different questions, which tap the domains of (a) hazardous alcohol use, (b) dependence symptoms, and (c) harmful alcohol use (Babor et al., 2001). To this end, it has been estimated that the AUDIT is over 90% effective in detecting persons with an alcohol use disorder (Bradley et al., 2003; Brown et al., 1997). Indeed, it has been identified as being superior in performance to the CAGE and the MAST in a variety of clinical settings, and appears to be valid for both male and female respondents (Babor et al., 2001). However, the AUDIT tends to miss active drinkers over the age of 65 (Isaacson & Schorling, 1999), and is not appropriate for use with adolescent drinkers (Knight, 2005). Another limitation of the AUDIT is that it is designed for use in detecting alcohol use disorders, and not for other forms of substance misuse. It cannot isolate current drinking patterns from past alcohol use patterns, and, finally, the intent of the items on the AUDIT is easily discerned, and thus the test is subject to dissimulation if this is the intent of the individual (Stein & Rogers, 2008). There is an abbreviated version, known as the AUDIT-C, which consists of only three questions, but available evidence suggests that the full AUDIT might be more effective than the abbreviated version (Holzel, Weiser, Berner, & Harter, 2008).

A popular screening instrument is the Substance Abuse Subtle Screening Inventory-3 (SASSI-3) (Juhnke, 2002).

This is a copyrighted instrument that can either be computer- or hand-scored. It is administered to individuals who are at least 16 years of age, and who have at least a fourth-grade reading level. It takes about 15 minutes for the client to take the SASSI-3, and it provides measures on 10 different scales, including two “truth” scales. Some of the items are quite obvious in intent, while others are rather subtle. Though it can be hand-scored, the computer-administered/scored version is becoming increasingly popular with the widespread use of desktop computers. While the SASSI does not provide data on which substance(s) the individual might misuse, it does provide a score that suggests that the individual is or is not likely to have a substance use disorder.

A screening tool that is useful for the identification of substance misuse is the Drug Abuse Screening Test (DAST). This instrument is rapidly administered, usually in 5 minutes or less, requires a sixth-grade reading level, and excludes alcohol use. The DAST was modeled after the MAST, but focuses on illicit drug use. It is composed of 20 questions that are answered either “yes” or “no.” It was originally intended for use with adults, but a modified form has been developed for use with adolescents. Scoring is easy, as 18 of the 20 items are scored as “hits” if the individual responded “yes,” and the other two are scored as “hits” if the individual responded “no.” A score of seven or more points suggests a substance use disorder. A disadvantage of the DAST is that the intent of the items is readily apparent, allowing the individual to lie about his or her substance misuse if motivated to do so.

The utility of screening instruments in the detection of alcohol or drug use disorders has been challenged (“California judges get tougher on science,” 1997). However, they do provide one piece of data in a comprehensive assessment process using multiple data points to arrive at a diagnostic formulation. One such data point might be one of the semistructured clinical interviews designed to allow the clinician to obtain the data necessary to adequately determine whether there is a substance use disorder present. These semistructured screening instruments usually focus on the diagnostic criteria utilized by the American Psychiatric Association (2013).

An instrument often administered during the screening process is the Beck Depression Inventory (BDI). While the BDI does not address substance use issues, it does provide an objective measure of the client’s depression, which may form the basis for a referral to a mental health professional for evaluation and treatment, and, since the drugs of misuse can often cause or contribute to depression, lead to further inquiry into the reasons the client is depressed. A man with a high score on the BDI, which suggests high levels of depression, might reveal upon inquiry that his wife took the children and moved out because of substance-related conflict

between them, or that he just lost his job, to cite two possible examples. The BDI and its revisions are copyrighted instruments that are easily administered and scored in just a few minutes.

One instrument that is often utilized as a screening tool is the Minnesota Multiphasic Personality Inventory (MMPI).⁴ The original MMPI was introduced in 1943, and the MacAndrew Alcoholism Scale⁵ was introduced in the mid-1960s after an item analysis suggested that alcohol-dependent individuals had a tendency to answer 49 items of the 566 items differently than nonalcoholic persons. A cut-off score of 24 items answered in the “scorable” direction correctly identified 82% of alcohol-dependent persons in a sample of 400 psychiatric patients (Graham, 1990). In 1989, the venerable MMPI was updated, and the Minnesota Multiphasic Personality Inventory-2 (MMPI-2[®]) was introduced. The “Mac” scale was slightly modified, but essentially retained its original form. Currently, the modified Mac scale is thought to be about 85% accurate in the detection of substance use disorders (Craig, 2004). Because of the shortcomings of the Mac scale, it should be used as one piece of data, and by itself should not be interpreted as evidence of a substance use disorder.

Following its introduction, it was suggested that the MMPI-2 Mac scale identified personality patterns more commonly associated with substance use disorders than the actual SUDs (Rouse, Butcher, & Miller, 1999). Clients who are extroverted, who experience a blackout for any reason,⁶ who tend to be more assertive, or who enjoy risk-taking behaviors tend to score higher on the Mac scale, even if they do not have an SUD (Graham, 1990). Further, in spite of the validity scales built into the MMPI-2, Otto, Lang, Megargee, and Rosenblatt (1989) discovered shortly after the revised MMPI was introduced that alcohol-dependent persons might be able to “conceal their drinking problems even when the relatively subtle special alcohol scales of the MMPI are applied,” through either conscious or unconscious denial (p. 7). Finally, taking the MMPI is time-intensive, which does not make it a convenient test for screening purposes. The MMPI is, however, of use in the *diagnosis* stage of the assessment process.

Section Summary

The process of screening for a substance use disorder can involve a verbal, face-to-face interview, the use of various screening

⁴The MMPI and the MMPI-2 are both copyrighted instruments.

⁵Also known as the “Mac” scale.

⁶For example, a person who has a seizure disorder.

instruments, or, ideally, a mixture of the two. At the end of this process, the clinician should be able to determine whether there is evidence of a substance use disorder or not. If there is no evidence of an SUD, then the screening processes ends at this point. However, if there is evidence of an SUD detected, then the clinician moves on to the next stage: assessment.

Assessment

If the screening process suggests that a substance use disorder is present, it is during this phase that the clinician attempts to measure the severity of the individual's substance use disorder. There may be a smooth transition to the assessment phase, or it could be an abrupt shift, with assessment occurring at a later time, depending on the setting where the screening was conducted. For example, if a client was screened while in the ER, then referred for an assessment at a treatment facility, the process may be much different than if the person is being screened and then assessed at the same place, by the same clinician.

The assessment process is certainly about gaining more specificity. As was covered in the previous section, screening has limitations, especially in relation to understanding the extent of the struggles of an individual. As Gitlow (2011) observed, the diagnosis of a person having an SUD says little about the quantity or frequency of that person's misuse of chemicals. An analogy might be a person who has lung cancer and who is treated with a combination of surgery and radiation therapy. Even if there was no sign of recurrent tumors, the diagnosis of "lung cancer" would stay in the patient's chart, although with the modifier "apparent surgical cure [and a specific date]."

It is the duty of the assessor to strive to be as accurate as possible, always being cognizant of the process of **diagnostic inflation**, which is sometimes the unfortunate outcome of the process when a poorly trained clinician or vague diagnostic criteria result in ever-growing numbers of people being diagnosed with a condition that in reality they do not have. This results in unnecessary referrals for treatment and blocks access to the available treatment resources for those who do need rehabilitation.

After introductions, the assessor explains that the purpose of the interviews is not to assign blame, but to help the assessor gain an understanding of the interviewee's life and where their chemical use fits into their lifestyle. Many assessors find that it is less threatening to ask the client to describe his or her life five years prior to the meeting. The focus of this is to establish a baseline about the individual's general lifestyle at that time. At some point during the discussion, the client is also asked to describe what his or her substance use

history was like at that point in life, or if recreational chemical use had ever caused them problems before that point. The client is then asked to describe his or her lifestyle 2 years prior to the present time, and the role that chemical(s) played in life then. Finally, the client is asked to describe his or her current lifestyle, and the role of chemicals in their present life. Using a technique borrowed from motivational interviewing, the individual should be asked whether he or she believes that the use of chemicals is or was a problem for him or her at each stage of life discussed, and why (or why not) he or she believes this. If at any point in time the client reported abstaining from chemical use, the assessor should inquire about the circumstances to which the client attributed his or her abstinence, as well as the return to chemical misuse.

An important point that must be assessed is *whether the client has ever experienced a substance withdrawal syndrome*, taking care to describe the symptoms of a withdrawal syndrome from the substance(s) that the individual is thought to have been abusing, either in the recent or remote past (Greenfield & Hennessy, 2008). This is not definitive proof that a person is addicted to a compound(s), although it is strong evidence that the individual is at least a heavy misuser of that substance(s), and underscores the need for an in-depth assessment of the individual's substance use patterns. The assessor must remember that the same disorder might have far different presentations as the disease progresses (Greenfield & Hennessy, 2014). The end-stage alcoholic, for example, will have a different clinical presentation than the young adult drinker who is misusing alcohol. Both might present different clinical pictures than the person who was cocaine dependent but who had not misused alcohol or illicit substances in the past decade.

There are three formats for the assessment process: (a) unstructured, (b) semistructured, and (c) structured. The clinical interview is usually an unstructured assessment process which might be an extension of the screening interview outlined above if it becomes apparent that the individual has an SUD. A weakness of the semistructured and structured interview manuals in use is that they do not permit elaboration on atypical responses. These are some of the reasons why Juhnke (2002) identified four benefits of the clinical interview over semistructured and structured interviews:

1. flexibility
2. establishment of rapport with the client
3. reassurance to clients uncomfortable working with written tests or computers (if the test is administered on a computer)
4. allows the therapist to watch the client's nonverbal behavior in response to question(s), to identify areas for subsequent exploration

As was noted above, the assessor should assure the client that the purpose of the interview is not to assign blame, but to help the assessor obtain a better understanding of the interviewee's substance use. The assessor will also explain that *specific* responses would be most helpful. At this time the assessor might want to explain that many of these questions might have been asked of the client by others in the past; however, this information is important, and so the assessor will request the information from the client again. The client is provided with the opportunity to ask any questions s/he might have, and then the interview process begins. It is not uncommon for the interview to take place within a framework provided by the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5), although other formats, such as the one utilized by the American Society of Addiction Medicine (ASAM), might also be utilized. Each of these diagnostic manuals provides certain criteria within which the individual's substance use disorder might be evaluated, and provides a common language that health care professionals understand.

The information the client offers (or elects not to offer) during the clinical interview is a valuable component of the assessment process. However, this data is also vulnerable to one of four different "response sets" that might distort the assessor's opinion of the client's substance use disorder (Stein & Rogers, 2008): (1) *Disacknowledgment*: The individual repeatedly offers "I don't know" or "I can't remember" responses to questions that might reveal incriminating information. (2) *Misappraisal*: The client might honestly mistake the amount ingested (client reports consuming three or four drinks, whereas collateral information sources report that the client had ingested eight mixed drinks on a given night). (3) *Denial*: The client might be motivated to avoid consequences of substance use behavior such as legal sanctions. Finally, (4) *exaggeration*: The intentional over-reporting of substance use, often seen in adolescents who misuse substances who use this as a cry for help. Criminal offenders might utilize this form of distortion to try to establish grounds for a claim of mitigating circumstances at the time of sentencing if they have legal charges pending, for example.

The myth that individuals who misuse substances will automatically lie about their substance use is often repeated as clinical fact by many professionals within the SUD field. It is possible that a given person will be less than honest about his or her substance misuse, especially if he or she believes that the information that is revealed might be used against him or her later (Fletcher, 2013). This does not apply only to situations where a person is facing possible legal charges: As Frances (2013) pointed out, on occasion a person's diagnosis can be wielded like a sword in family feuds. It is for this reason that the assessor should consider the referral source

for the individual being assessed. For example, if the client is being seen as part of a child custody evaluation or pre-employment evaluation, the individual might either consciously or unconsciously distort the information he or she provides to the assessor. Collateral information (past treatment records, court documents, information from family members, etc.) often either corroborates or uncovers distortions in the individual's history.

It is useful for the assessor to ask questions during the interview that are designed to explore the same client response from different perspectives. This is done to provide a form of internal validity to the data obtained during the clinical interview. For example, the client might be asked, "In the average week, how often would you estimate that you use alcohol or drugs?" At a later point in the interview, the assessor might ask, "In the average week, how much would you say that you spend on alcohol or drugs?" If there is a discrepancy, the assessor will want to explore it. Clients who report using alcohol just once a week, but who claim to spend \$100 a week on recreational substance use might respond that they always buy drinks for their friends when they go out to drink, or that they have a gambling or substance use disorder other than alcoholism.

One point that the assessor will wish to consider is the *estimated percentage of his/her income spent on alcohol or drugs*. If the client is receiving unemployment compensation checks for \$200 each week, for example, but is spending \$50 a week on alcohol or drugs, then s/he is spending a significant percentage of his/her income on substances in spite of their employment status. In contrast to this is the client who makes \$2,000 a week, but who spends \$15 each week on beer, which provides evidence of a far different pattern of drinking.

An indirect source of collateral information is *medical test data*, a topic that will be discussed later in this chapter. There are no current blood or urine tests specific for detecting an SUD, as even if a substance is detected in the individual's urine or blood at a given time, this does not mean that the individual is a *chronic* user. It only means that the substance was in his or her blood or urine at the time of the test. However, a series of positive blood or urine test results makes it far harder for the client to argue that s/he does not misuse chemicals. Further, urine toxicology tests can determine whether prescribed drugs that should be in the client's system were present, although they cannot determine the amount of the compound in the client's body. Finally, the appropriate blood or urine tests can help identify concurrent medical disorders that might complicate efforts at treating the SUD (for example, an untreated infection or heart problem) (Work Group on Substance Use Disorders, 2007).

Psychological test data may directly or indirectly assist the assessment process. A number of instruments have been

discussed elsewhere in this chapter that are of value in the screening and assessment process. A major disadvantage of paper-and-pencil and computerized tests is that they are subject to denial, distortion, and outright misrepresentation on the part of the client, and thus are better suited to situations where the client is unlikely to “positively dissimulate” (Evans & Sullivan, 2001).

Psychological test data might offer help in identifying client personality characteristics that might influence his/her substance use pattern. A depressed client, for example, might be using alcohol or drugs to self-medicate depressive symptomatology, although the reverse is also possible: The observed depression might be substance-induced. Although psychological tests other than those directly developed for screening or assessment of substance use disorders can offer little direct evidence that problems exist (“California judges get tougher on science,” 1997), they can identify aspects of the problem that might have been overlooked otherwise.

The assessor must not make assumptions about the client’s responses. If a client reported “only this one arrest” for a drug-possession charge, the assessor must not make assumptions. Rather, the assessor must ask questions such as, “What about in other states or countries?” or, “Were there any substance-related charges brought against you while you were in the military?” The client’s responses may be revealing.

Standardized Tests^{7,8}

Although the clinical interview forms the cornerstone of the assessment process, the assessor should also utilize standardized test results as an aid in the assessment process (Juhnke, 2002). The client’s responses will become a part of the database upon which the assessor draws for the final stage of the assessment process: the diagnosis (discussed later in this chapter). Such self-report instruments provide a comparison between the individual’s characteristics and those of patients who have been identified as misusing substances and who have benefited from intervention(s) (Samet, Waxman, Hazenbuehler, & Hasin, 2007).

One popular instrument used for individuals over the age of 16 is the *Alcohol Use Inventory* (AUI; Horn, Wanberg, & Foster, 1990). This copyrighted instrument is composed of

228 items, and it takes 30–60 minutes for the individual to finish. The test data then is then interpreted across 24 domains to help the assessor better understand the client’s alcohol use pattern. Unfortunately, the AUI is limited to alcohol use disorders. Further, the normative data for the AUI make it inappropriate to use with certain subgroups.

The *Addiction Severity Index* (ASI; McLellan, Luborsky, O’Brien, & Woody, 1980), on the other hand, is a public domain instrument that forms the core of a semistructured interview with the client. There are 200 questions in the fifth edition of the ASI, each of which the interviewer will ask the client while recording his/her responses, although it can be taken in a written or computerized format as well. The ASI is useful in the assessment of SUDs other than alcohol use disorders, and measures such areas as the client’s interpersonal relationship patterns, possible medical problems, legal history, etc. (Samet et al., 2007). The client is asked to rate his/her level of distress on each domain from 0 (no distress) to 4 (extreme distress), while the assessor also notes areas that should be addressed through professional intervention. While useful, the normative population for the ASI were patients in the Veterans Administration hospital system, and this instrument has been found to have limited validity in working with special populations such as the homeless or clients with concurrent substance use and mental health problems⁹ (Monti, Kadden, Rohsenow, Cooney, & Abrams, 2002; Samet et al., 2007; Stein & Rogers, 2008).

The *Structured Clinical Interview for DSM (SCID)* was originally developed by Riskind, Beck, Berchick, and Brown (1987) to follow the *DSM-III*. It has been since revised, and the newest version, the *SCID-5* (First, Williams, Karg, & Spitzer, 2015), is an instrument available in different forms for researchers and other forms for clinicians (Samet et al., 2007). The clinical version of the SCID requires training as a therapist, and is a semistructured instrument that will allow the assessor to explore client responses that might require clarification. It is applicable to both alcohol use and substance use disorders, but it can require up to several hours for the therapist to administer to the client, depending on his/her status and level of function. Fortunately, it is designed to be administered in a series of modules, and the clinician may utilize only those modules that are of relevance to that client (Samet et al., 2007).

The *Drug Use Screening Inventory—Revised* (DUSI-R; Tarter, 1990) assesses multiple domains: (1) drug use, (2) psychiatric, (3) behavioral problems, (4) school adjustment, (5) health, (6) work adjustment, (7) relationships with peers, (8) social competency, (9) family adjustment, and (10) leisure

⁷There are a number of assessment tools that have been devised for research studies, but which are not used in clinical practice. These tools will not be discussed in this text.

⁸The author is frequently asked to render an opinion as to the best test or instrument to use. There is no single test that is universally accepted, and each has certain strengths and weaknesses. A site that may be useful to the reader is the Substance Use Screening & Assessments Instruments Database, maintained by the University of Washington: <http://lib.adaa.washington.edu/instruments/>.

⁹Discussed in Chapter 25.

activities. While this instrument provides a great deal of useful information, it is not popular at this time.

Section Summary

In this section, some of the more popular paper-and-pencil and computerized assessment instruments currently in use are reviewed. These instruments form part of the database on which the assessor will base his or her conclusions. However, they do not take the place of a formal clinical interview, and the clinician should not base his or her diagnosis only on the test results.

The Assessment Format

There is no standardized format for the assessment process. Rather, the format utilized for the assessment process will vary depending on the needs of the assessor and the facility for which s/he works. Assessments need to be sensitive to the cultural beliefs of the client, and one needs to be aware that different cultural groups might have different beliefs about substance use than the dominant culture (Greenfield & Hennessy, 2014). Frances (2013) offered a “stepped diagnosis” (p. 222) approach to psychiatric assessments, which he summarized in the following manner:

Step 1: Gather baseline data.

Step 2: Normalize problems. Take them seriously but consider the possibility that the behaviors in question were a predictable response to the stressors of everyday living.

Step 3: Watchful waiting: Continue the assessment process without having a preconceived diagnosis. Diagnostic impressions at this point should be tentative and considered in light of the data, and treatment efforts should be minimal and open to modification as events unfold.

Step 4: Minimal intervention: Structured interventions such as available computer based self-help groups, assigned reading, psycho-educational groups.

Step 5: Brief counseling.

Step 6: Formation of final diagnosis and initiation of appropriate treatment(s).

Admittedly, Frances’s (2013) assessment recommendations were designed for work with psychiatric patients as opposed to individuals misusing substances, but there are lessons the assessor might learn from this model. For example, the person who is being assessed after being arrested for driving under the influence of intoxicants and whose substance misuse was apparently a reaction to the unexpected death of

a spouse or child, and who did not demonstrated any sign of a substance use disorder before this tragic life event, is far different from a person with a long-standing history of substance misuse (see Step 2). However, there are some common elements among the better assessments, which will be reviewed below.

Circumstances of Referral

Why is this client here today? Individuals with an SUD will only rarely come in for help on a voluntary basis; they are usually forced into the assessment and subsequent rehabilitation program through external pressure (Craig, 2004). Thus, the manner in which the client answers the question, “What brought you here today?” will offer valuable information about his/her willingness to participate in the assessment process, evasiveness (or honesty), level of function, understanding of the problem(s) that s/he is facing, etc.

Substance Use Patterns

These should have been identified in the assessment phase, but the assessor should identify the grounds on which the client’s self-report is or is not assumed to be accurate. For example, a client who claims to have been alcohol and drug free for the past nine months (but who was incarcerated for that period of time) may be demonstrating some degree of denial and evasiveness, which would justify the use of collateral information sources. The assessor thus must determine the client’s current living situation, whether s/he is under the supervision of the courts (or incarcerated), and the client’s beliefs about his/her substance use. It is not uncommon for a client to proudly boast that it is only when he or she consumed liquor that he or she gets into trouble, so continued beer use is not a problem.

Past Treatment History

This is relevant for a number of reasons. Past research has shown that approximately half of those entering treatment for an alcohol use disorder (AUD) are entering treatment for the first time (LoCastro, Potter, Donovan, Couper, & Pope, 2008). First-time treatment participants for AUDs have significantly different alcohol use histories than do those being admitted to treatment for the second or third time. The social context of their alcohol use, needs, motivation for treatment, expectations, and health status will be significantly different than for the typical individual who has been admitted to treatment for an AUD more than once (LoCastro et al., 2008).

Individuals who are entering treatment for the first time tend to drink less per occasion of drinking, are probably less

knowledgeable about the nature of substance use disorders, are less likely to acknowledge the severity of their SUD, and are less likely to accept total abstinence as a viable treatment goal (LoCastro et al., 2008). They are also more likely to be younger, male, and employed at the time of their admission to treatment (LoCastro et al., 2008).

Clients who have been in treatment programs in the past might be “treatment wise,” an observation that is indirectly supported by the observation by LoCastro and colleagues (2008) that the treatment-naïve group in their study appeared to have less motivation for change than did the treatment-experienced group. They were more likely to reduce their level of alcohol use prior to admission to treatment (LoCastro et al., 2008). This suggests at least the possibility that the latter group knew the right words to say to impress staff with their willingness to “change,” although it is possible that they were indeed motivated to make life changes supportive of abstinence.

The client’s past treatment history also provides an indirect measure of the severity of the client’s SUD. A client who claims not to have a serious substance use disorder, but who has been in a rehabilitation program three different times, is providing information that is quite contradictory, and that might be signaling that s/he really will not be very cooperative with any efforts at rehabilitation. Thus, a review of the client’s past substance use treatment history is important.

Legal History

Increasingly, court conviction records are available through the internet. Such records, or records provided by the court, reveal (a) the nature of legal charges brought against the client in the past, their disposition, and possibly (b) the nature of any current charges pending against the client. It is important to keep in mind that the original charges might have been reduced through the process of plea negotiation(s). Thus, the client who had been arrested for possession of 6 ounces of marijuana might have been convicted of possession of less than an ounce by the court through plea negotiations. Also, a computer-based background check might reveal that a given client has charges pending in another state that have yet to be resolved, or a string of previous arrests that he or she failed to mention. Thus, checking the accuracy of the client’s self-report about his/her legal history against collateral information provides information about the relative accuracy of his/her self-report in general.

Past Military Record

One very important, and frequently overlooked, source of information about a client is his/her past military history

(if any). Some clients will only report legal convictions from their civilian record, ignoring charges and convictions from their military service. It is important to keep in mind that “reprimands” in the military often function as a form of plea negotiation, avoiding formal legal charges as would be brought against the individual by a court martial trial.

If the client should deny having ever been in the military, it might be of interest to determine *why* s/he never enlisted. A client who responds “I didn’t want to enlist” is possibly far different than the client who responds “I couldn’t enlist because I had a felony conviction on my record!” Finally, the client’s discharge status should be discussed. A client who has an honorable discharge might be far different than the client who received a general discharge under dishonorable conditions or just a dishonorable discharge from the military. Finally, the assessor should keep in mind that military discharges might result from medical disabilities or injuries, and thus are not automatically a sign that the individual’s military service was marked by conflict with the authorities.

Educational/Vocational History

This information, based on the client’s self-report and available records, provides data on the client’s level of function, and whether their chemical use has interfered with educational/vocational experiences to date. The client who reports that s/he “just barely graduated” from high school because s/he had trouble with the classwork is far different than the client who reports that s/he “just barely graduated” because s/he was under the influence of alcohol or drugs so often. Both hypothetical clients also present a far different clinical picture than the client who holds a bachelor of science degree.

The degree to which the client’s substance use might have interfered with his/her vocational history should also be explored. Many substance-misusing clients report that they are “self-employed,” which for them might be a subtle way of saying that they cannot hold a regular job because of their substance use disorder. Thus, the individual’s success as a self-employed worker should also be discussed. For employed or self-employed clients, their employment history should be explored in detail. Why did the client leave each job? Did they leave a given job because their substance use made it impossible for them to continue to work there, or because they were offered a promotion with a different company?

Developmental/Family History

Discussion in this area is often a treasure trove of information about the client’s early history and the environment that s/he grew up in. It also provides a chance for the assessor to explore how the client feels about his/her parents, whether

they had substance use disorders of their own, how they addressed them (if they did), whether either parent had a disability of any kind, or whether either parent died while the client was growing up. A client who hesitates to say that his or her father was alcohol-dependent, but compromises by saying that he was “a problem drinker” might also be hinting that s/he would hesitate to apply the same term to her/himself, if asked. An exploration of the developmental history might reveal that several siblings also have SUDs, which is a significant piece of information. Parental alcohol/substance use disorders might hint at a genetic predisposition¹⁰ toward an SUD, as well as possible modeling behaviors on the part of the parent(s) that might make the child more accepting of personal substance misuse. A discussion of the client’s home environment would also suggest how permissive or strict his/her home was, whether the client has unresolved feelings of anger toward a parent who had an SUD, and even possibly hint at self-hatred issues now that the client has developed an SUD just as the parent struggled with years earlier.

Psychiatric History

It is amazing how often assessors overlook the client’s past psychiatric history. Clients have been known to be hospitalized for such problems as a “brief reactive psychosis” or “atypical psychosis,” only to later reveal that they had been abusing a hallucinogenic substance that caused a bad reaction. All too often, when asked, these clients admit that nobody ever asked them whether they had used any drugs, and that a toxicology test to detect possible drug use was never performed.

It is important to inquire about whether the “suicidal” client had been using alcohol or drugs prior to being admitted to the hospital for suicidal thinking or an attempted suicide. *This does not imply that the client might not be a legitimate suicide risk!!!* However, the client’s motivation for making the suicide threat or attempt should be fully explored. If possible, the assessor should also obtain a copy of the client’s discharge summary, if not the entire treatment record, from the facility where he or she received psychiatric treatment.

Medical History

This topic often overlaps with the client’s psychiatric history. However, the assessor needs to explore the client’s medical history (Gendel, 2006). A history of a past hospitalization for treatment of internal injuries sustained in a motor vehicle accident might hint at a possible alcohol- or drug-related

accident that the client failed to report earlier in the assessment process. A client might deny having any substance use disorder, but admit that s/he had been shot twice by rival drug dealers in the past 3 years, two pieces of information that must be reconciled during the assessment.

The assessor should inquire about any current or recent prescription medications. It is also important for the assessor to identify those clients who might have been “doctor shopping”¹¹ to obtain desired medications, how many different health care providers are involved in the patient’s care, and whether these individuals are aware that the client had consulted the other(s) for care. Over-the-counter medication use should be discussed as well, since such medications can exacerbate problems caused by prescription medications, alter the pharmacokinetics of prescribed medications when used concurrently by a client, and have a misuse potential of their own.

Finally, the individual’s *expectations* for their drug(s) of use should be reviewed. For example, Reich and Goldman (2005) found that high-risk and low-risk alcohol users appear to have different expectations for the outcome of alcohol use. As a group, high-risk drinkers tended to anticipate a more positive outcome from their use of alcohol. Low-risk drinkers were more likely to expect more negative outcomes of their alcohol use, especially in terms of the level of sedation and alcohol’s negative impact on their social skills. Thus, the assessor should discuss the individual’s expectations for their drug(s) of misuse to determine what role they play in the person’s life.

Real Versus Pseudo-Personality Disorders

One point that is often overlooked by assessors is that long-term substance misuse requires that the individual’s personality adapt to the continued misuse of the chemical. The behaviors noted during the clinical interview, or in the client’s past while she or he was abusing chemicals, might not reflect the client’s core personality. The assessor must try to distinguish the client’s core personality from those characteristics that evolved as a response to their SUD (Grekin, Sher, & Wood, 2006). The possibility of a substance-induced pseudo-personality disorder must be considered by the assessor.¹² For example, Vaglum (2003) suggested that between 20 and 40%

¹⁰It should be emphasized out that a suspected genetic predisposition is not the same as a genetic *cause* of the person’s substance use disorder.

¹¹A term applied to the process of looking for a physician who will prescribe a desired medication. Sometimes, this might require that they see two, three, four, or even more physicians before they find one willing to diagnose them with a condition that makes their use of a desired medication legitimate. Substance-abusing clients have been known to study what symptoms they need to report/demonstrate in order to convince the physician to prescribe a desired medication.

¹²At this point the reader is welcome to groan in frustration, or despair.

of individuals with OUDs who were diagnosed as having an antisocial personality disorder actually engaged in antisocial behaviors because of their addiction, but that they did not have an antisocial personality disorder prior to the development of their SUD. It is not uncommon, for example, to hear a client tell a therapist or a treatment group that “I never thought that I would reach the point where I would not [do X], but, well, I did it.” In this hypothetical case, the substance of choice forces the individual to engage in previously forbidden behaviors to allow him or her to continue to misuse chemicals.¹³ Frequently, a careful history will reveal that the individual being assessed was forced into a pattern of antisocial *behavior* to support his or her SUD without having an ASPD. One determining factor is whether the personality pattern that the client presents *predated* the development of the SUD or was a *consequence* of the SUD (Grekin et al., 2006). The differentiation between real and substance-induced personality disorders is of major significance, since this has profound implications for the individual’s rehabilitation.

Section Summary

On the basis of the information obtained through the clinical interview, collateral information, and test data, the assessor will be in a position to determine where on the continuum of substance use disorders identified in Chapter 1 the client appears to fall, based on available evidence.

The Assessor and Data Privacy

The issue of confidentiality has always been a difficult one, and recent changes in state and federal data privacy laws have served to make matters even more complicated.¹⁴ Many clients fear, for example, that their parents, spouse, employer, law enforcement agencies, or professional licensing boards will have access to the records, making them hesitant to discuss problems or concerns openly. The assessor will need to review the data privacy laws with the client, so that he or she knows in advance who will, and will not, have access to his or her records. It will also be necessary for the assessor to discuss the conditions under which information provided by the client might be released.

To further complicate matters, the data privacy rules addressing therapy or assessment sessions with a child or adolescent might be different from the laws that apply to sessions with an adult. In some areas, adolescents above a certain age might request professional services that, while the parent is obligated to pay for such sessions, are still protected information that cannot be discussed with the parent (Greenfield & Hennessy, 2008).

Traditionally, information revealed by or about a patient is considered privileged and protected. There are exceptions to this rule, however. If a patient were to reveal that he or she was actively abusing a child, the clinician might be obligated to report this to the authorities under what are known as “duty to report” laws. Another exception to the privilege of confidentiality involves cases where the individual reveals specific plans to harm him/herself or another person. In such cases, proper steps must be taken to protect the client and the potential victim(s). There are states in which the court is permitted to order that certain information be released to the court, usually when that information is relevant to an ongoing legal investigation.

Clients will frequently reveal that they have been in a treatment program on previous occasions, and these treatment records are useful adjuncts to the assessor. To obtain copies of these treatment records it will be necessary for the assessor to obtain a *release of information authorization* from the client. This is a written form signed by the client that gives his or her permission for one facility to release information to another facility. The client also has the right to specify *which* information can be released by a facility. This type of form should also be used in situations where family members or other collateral contacts are made, as the permission of the client is necessary in most instances. Finally, the client has the right to refuse to even talk to the assessor if he or she should so choose. The privilege of confidentiality is always the client’s, except under very specific circumstances, and is not breached lightly.

When the final evaluation report is composed, the assessor should identify the exact source(s) of information utilized in the formulation of the report. Collateral information sources should be notified in advance that the client, and/or the client’s attorney, has a right to request a copy of the final draft of the report, and thus their contribution to the final draft of the report might become known to the client. Further, although it is rare, on occasion the client does request a copy of the final report, and technically has a right to do so, after filling out the proper release of information authorization forms.

Diagnostic Rules

Many individuals will resist a diagnosis of a substance use disorder, at least at first. Because of this, there are two diagnostic rules that the assessor should adhere to as much

¹³An interesting point to debate is whether the individual who is unwilling to make this adjustment (unwilling to “pay the cost” for their addiction) is characteristically protected against the development of an SUD.

¹⁴It is recommended that the reader consult an attorney to discuss what data privacy regulations apply in their specific state, and review the relevant state statutes as well as the federal guidelines that also must be kept in mind. One relevant federal law is the *Health Insurance Portability and Accountability Act* (HIPAA).

as possible. First, always gather collateral information. As a group, those with SUDs will be reasonably accurate about their substance use, especially if sober when they are asked about their substance use patterns. There are exceptions to this rule, however, such as when the individual is facing the threat of legal action (Gendel, 2006). A person facing the possibility of a long prison or jail sentence may exaggerate his or her self-report of having an SUD, not because it is true, but because it might serve as a mitigating factor that could reduce the severity of his or her sentence. In contrast to this, clients with co-occurring disorders often under-report the extent of problems caused by their substance use disorder because they fear loss of entitlements (Social Security, etc.).

One advantage of collateral information data is the determination of whether the client's reported behavior when under the influence of a compound is consistent with the known characteristics of that compound. Collateral information sources might support the client's claim of atypical effects from a drug(s) of misuse, or deny that the client even used alcohol or drug(s) at times when the client claims otherwise. Every assessor has experienced the scenario in which the client claims to use alcohol "just once a week, perhaps not even that often." When asked, the spouse admits that the person uses alcohol nightly, drinking to the point of intoxication every night after work. Obviously, time constraints limit the assessor's ability to contact collateral sources of information to some degree. If the report is due in 72 hours, it might not be possible to contact collateral information sources, but an attempt should be made after obtaining the proper release of information authorization. Collateral information sources might include:

1. the patient's family
2. friends of the patient
3. employer or coworkers
4. clergy members
5. local law enforcement officials (criminal convictions are public and can be accessed over the internet)
6. primary care physician and other medical professionals
7. psychotherapist or family therapist (if any)

It will be of value to note whether the collateral information sources cooperate or if they refuse to cooperate. It should also be noted whether the client was able to contact the collateral information source before the therapist to coach them on what to say. In more than one case, the assessor has heard the client in the background, telling the collateral information source how to answer the questions asked during a telephone conversation. This information should also be noted in the assessment report.

Rule number two: *Always assume deception until proven otherwise.* It has been found that *as a group*, those who are

alcohol dependent tend to be honest about their drinking pattern, but since there are exceptions to this rule, it is important to be cautious. One study, for example, concluded that 40% of individuals identified as drinking heavily lie to their physicians about the extent of their drinking ("Heavy drinkers 'lie to doctors,'" 2008). Further, clients might consciously or unconsciously distort information provided to the assessor, possibly because of their distorted way of thinking (Ross, 2002) or inaccurate information. The client who claims to be an "infrequent" drinker but who actually consumes five to seven beers each evening with coworkers at the end of the day might be attempting to deceive the assessor, or might actually believe that this constitutes "infrequent" drinking. After all, it is expected that he or she joins coworkers at the end of the day, and the individual might only consume alcohol on rare occasions other than with coworkers at the end of the work day.

Unconscious deception is a very real danger during the assessment process. A wise assessor will keep in mind that even "cooperative" clients might engage in such deception. One client might smugly report that she or he spends \$20 a week on alcohol. When confronted with the reality that this amounts to \$1,040 a year, that same client might become indignant and claim that she or he was spending *only* \$20 a week for alcohol because their denial system will not allow them to think otherwise. It is also common for the person to claim to drink "once or twice a week" until confronted with the fact that their medical problems are unlikely to have resulted from such a limited level of alcohol use.

It is important to ask not only about legal problems associated with the client's substance use in their home state, but also in other states and while in the military. A client who admits to one arrest for driving under the influence of alcohol might, when pressed, admit to other charges in other states, and defend their response on the grounds that they thought that the assessor "only meant this state," or that the client did not think those other convictions applied, since they happened while the client was enlisted in the military.

Other Sources of Information: Medical Test Data

There are no blood, urine, or other medical tests that will prove that a person is addicted to alcohol or drugs, despite this rapidly developing technology (ASAM, 2013). There are a variety of medical tests that can help determine what drug classes, metabolites, or specific drugs, including alcohol, are present in an individual's body, including urine, blood, saliva, sweat, hair, nails, and breath (ASAM, 2013). As stated

earlier, a single positive toxicology test does not, by itself, prove that the client has a substance use problem. A series of three or four positive samples is more definitive, and it is hard for a client to claim that the toxicology test was done right after his or her first experimental use of a chemical if they have three positive samples over two months!

Breath analysis might identify the blood alcohol level in the client's system, but not how long that individual has been drinking. Abnormal blood test results should serve as a warning that a patient *might* be misusing alcohol or illicit drugs. However, there are other potential causes of abnormal blood test results. For example, elevated liver function tests might reflect alcohol-related damage, or they might be caused by other medical conditions. Medical tests can often:

1. confirm the presence of certain chemicals in the patient's body
2. identify the specific compounds that are present
3. possibly determine the level of the chemical(s) in the patient's body
4. hint at how long the patient has been abusing chemicals

Further, the appropriate medical tests can identify concurrent medical disorders that might complicate efforts at substance rehabilitation, such as a cardiac problem (Work Group on Substance Use Disorders, 2007). As with all sources of information that one might use in the screening and assessment process, careful consideration of results is essential in how one sees such results contributing to the overall clinical picture of the individual.

Diagnosis: The Outcome of the Assessment Process

At the end of the assessment, the assessor should be able to answer four interrelated questions: (a) whether the individual does or does not have a substance use disorder, and the evidence on which that conclusion is based; (b) the *severity* of the individual's substance use problem; (c) the client's *motivation to change*; and (d) *factors that contribute/support further substance use* (Connors, Donovan, & DiClemente, 2001). In other words, the assessor should be able to make a *diagnosis* at the end of the assessment process and be progressing to treatment considerations next.

Many mental health professionals mistakenly believe that the American Psychiatric Association's (2013) *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (currently in its 5th incarnation) provides a tool for a comprehensive assessment of the substance use disorders. Like its predecessors, the DSM-5 does not identify the role that

a substance might play in the person's life or how to proceed with treatment decisions. The DSM-5 does suggest that some of the signs of a SUD include:

1. *Taking more of the substance than intended or over longer time periods*
2. *Desire to stop use or unsuccessful at cutting down or controlling use*
3. *Significant amount of time spent in acquiring, using, or recovering*
4. *Craving the substance*
5. *Using results in not fulfilling work, home, and/or school obligations*
6. *Using despite social or relationship issues caused or made worse by use*
7. *Reducing social, occupational, or recreational activities in favor of using that time for additional substance use*
8. *Continuing to use in physically hazardous situations*
9. *Continuing to use in spite of emotional or physical problems caused or made worse by the substance use*
10. *Development of tolerance*
11. *Developing withdrawal symptoms*¹⁵

If the client claims to be abstinent at the time of the assessment, it is necessary to determine the circumstances under which this abstinence was achieved. A client who claims to have abstained from all drugs of misuse for the past 4 months (while incarcerated for the last 4 months) presents a different clinical picture than the client who reports no alcohol or illicit drug use for the past 4 months while living independently. Clients who are under the supervision of the court system (or probation/parole officers) may abstain from alcohol and drugs because they are required to submit to urine toxicology testing on a random basis, for example. Thus, the assessor must determine why the client has abstained from chemicals, if she or he reports abstinence.

Although reaching the point of diagnosis is often viewed by clinicians as only a necessary step to ensure that an insurance company pays for the recommended treatment (and ensures the continued employment of the assessor!), in reality, it is far more than this. It is an ongoing process against which the client's needs, strengths, and resources should be measured on a day-to-day basis. Figure 28-1 depicts a flow chart of the assessment process.

In addition to an accurate diagnosis of the client's substance use pattern, the assessor should also be able to identify the individual's *motivation for seeking the assessment*. The client who is seen after being ordered by a probation officer to

¹⁵This material is reviewed for illustrative purposes only. See the *Diagnostic and Statistical Manual of Mental Disease* (5th ed.) for a complete discussion of the American Psychiatric Association's diagnostic criteria.

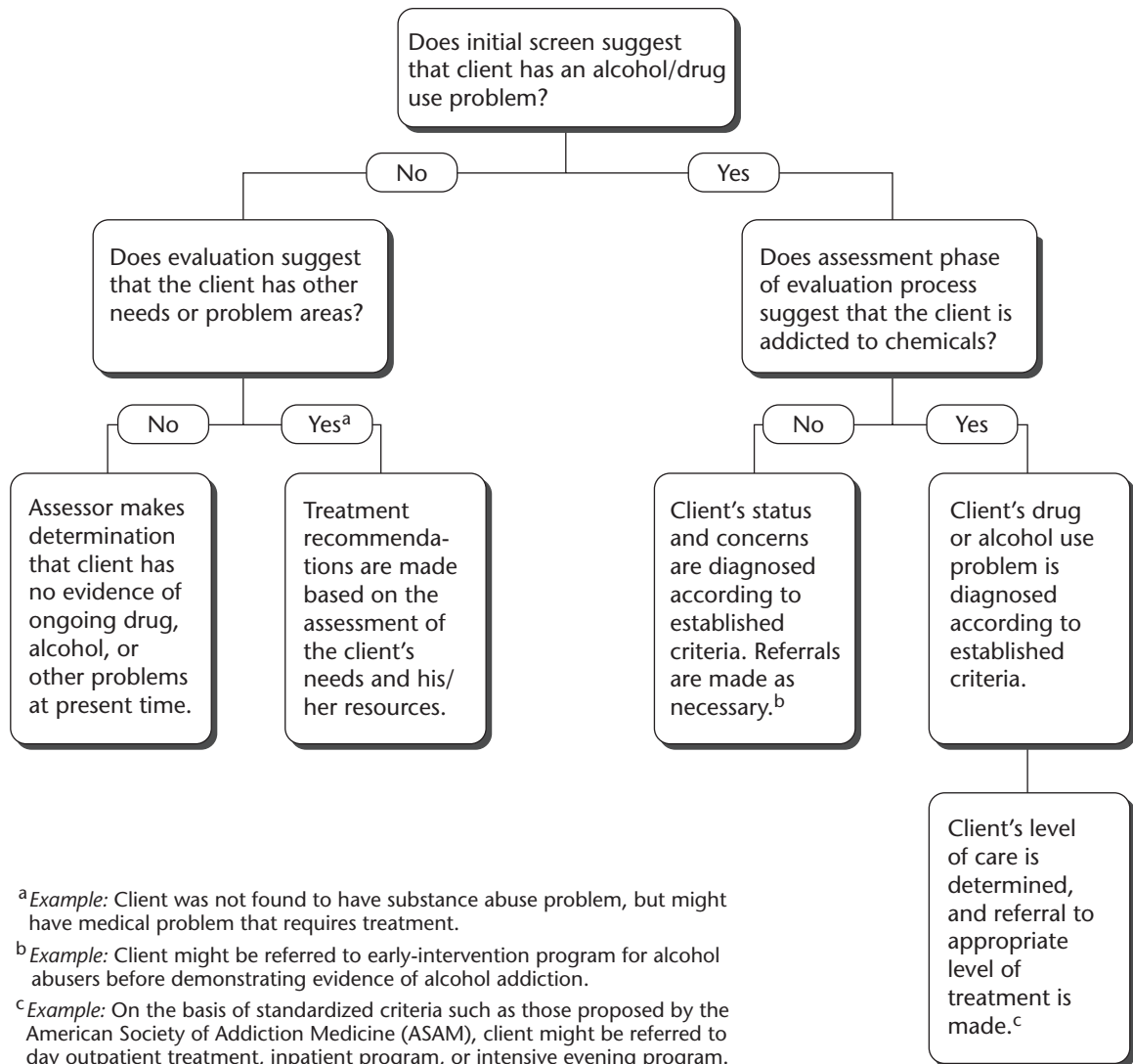


FIGURE 27-1 A Flowchart of the Assessment Process.

have the assessment offers a different level of motivation than does a person who seeks help because of substance-related life-threatening physical illness, and both individuals present the assessor with different forms of motivation than the person who is self-motivated to stop misusing alcohol or drugs.

It should be noted that some clients seek a substance use assessment and treatment recommendations not because they wish to come to terms with their SUD, but for *impression management* purposes (Wild, Cunningham, & Hobdon, 1998). Willingness to enter treatment for a substance use disorder does not automatically translate into willingness to change one's chemical use pattern (Connors et al., 2001). Individuals with pending court hearings on unresolved legal

charges, especially drug-related legal issues, might seek admission to treatment without any desire to do more than “look good” before the judge (“I have been through treatment, your Honor!”). Imagine, for a moment, a person who has been arrested for the crime of selling drugs, but who does not actually misuse alcohol or drugs.¹⁶ The question facing the assessor is whether to refer this individual to a substance treatment program when the client does not have such a disorder, or recommend that the client be referred elsewhere. While

¹⁶Yes, such people exist. Their motivation for drug sales is not to support their own substance use disorder, but to partake of the profits made through the sale of illicit drugs.

the majority of clients referred to a rehabilitation facility are there because of external pressure (wife, employer, the court system, etc.), the person who enters treatment for the sole purpose of attempting to manipulate the court system wastes valuable treatment resources better used to treat others.

Treatment Referrals

Having established that the client does or does not have an SUD, the next step is the determination of the *appropriate level of care*. The Work Group on Substance Use Disorders (2007) suggested seven criteria that should be considered when making a decision about the appropriate level of care for the client: (1) the individual's ability and willingness to participate in treatment, (2) the individual's ability to carry out self-care activities,¹⁷ (3) the individual's family and social environment, (4) the individual's need for structure to assist them in achieving abstinence, (5) their need for ancillary treatment for concurrent medical or psychiatric problems, (6) the availability of treatment programs in a given area, and (7) the client's preference for a specific form of treatment.¹⁸

The criteria offered by the American Society of Addiction Medicine (ASAM) also provide an excellent guide to determining the appropriate level of care for a given client (ASAM, 2001, 2013). The ASAM patient placement guide is not, in spite of widespread belief to the contrary, a comprehensive *assessment* tool. It is a guide to the appropriate level of patient care once the diagnosis of a substance use disorder has been established (Fletcher, 2013). This program guide has become the most commonly utilized system to determine clients' level of care needs (Gastfriend, 2004a, 2004b), and in some states its use is required by state law.¹⁹ The ASAM dimensions help to guide level of care considerations based on (a) acute intoxication/withdrawal potential, (b) health and current conditions, (c) emotional/behavioral/cognitive conditions, (d) readiness for change, (e) current use or relapse potential, and (f) living situation (ASAM, 2013). Another

factor that is rarely discussed is the client's legal status. The level of care decision might have been made by the court system, which will mandate a specific level of care for the client, and failure to complete treatment at that level will result in revocation of probation or parole. The most recent revision of the ASAM patient placement criteria identifies five main levels of care:

1. Level 0.5: Early intervention
2. Level 1: Outpatient treatment
3. Level 2: Intensive outpatient treatment/partial hospitalization
4. Level 3: Residential/inpatient treatment
5. Level 4: Medically managed intensive inpatient treatment

The ASAM patient placement criteria have been found to be effective by studies designed to test whether they stand up to "managed care" demands for specific level of care decisions (Mee-Lee & Gastfriend, 2008).

There are other systems available that will guide the assessor in making this determination. All of these patient placement guides are governed by the principle of the *least restrictive treatment alternative*, in which the client's strengths, needs, and his or her treatment history, potential for relapse, availability of a support system, etc. are reviewed to help determine the appropriate level of care (Work Group on Substance Use Disorders, 2007).

Chapter Summary

The evaluation process consists of three phases: (1) screening, (2) assessment, and (3) diagnosis. Each of these phases rests on the one before it, and closely parallels the medical diagnosis process. If there is evidence that a condition might exist (screening), it is then assessed. During the assessment process, the parameters of the condition, its duration, intensity, factors that might reduce its severity, and others that might exacerbate it are explored. At the end of the assessment stage, the assessor is in a position to make a formal *diagnosis* and to then make treatment recommendations. Included in the treatment recommendations is the level of care that would be most appropriate for the individual client. Some of the aids available to assessors for use in each stage of the assessment process were reviewed.

¹⁷Often called *activities of daily living*, or *ADLs*.

¹⁸While the client's wishes for a specific form of treatment should not dictate the level of treatment recommended, they should be taken into consideration by the assessor and if dismissed, a rationale for why they were dismissed included in the final report.

¹⁹Always consult with an attorney to determine in requirements in your state.



CHAPTER 29

Intervention¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 29.1** Understand the concept of intervention
- 29.2** Review the history of the intervention movement
- 29.3** Understand the characteristics of the intervention process
- 29.4** Describe the mechanics of intervention
- 29.5** Describe ethical considerations in relation to interventions
- 29.6** Review some common forms of intervention

The most promising way—perhaps the only way—to put enough addicts into treatment long enough to make a difference entails a considerable measure of coercion.

—Satel and Farabee (2005, p. 690)

Introduction

There are many who would challenge the validity of the above quote. There are also those who would defend its validity, in part because many persons with substance use disorders (SUDs) do not perceive the need for rehabilitation (Edlund, Booth, & Feldman, 2009) or believe that there is a stigma attached to entering treatment for an SUD (Fletcher, 2013). The subject of intervention has become widely acknowledged as a result of often dramatic television programs in which a counselor joins a family in confronting a family member with a substance use disorder (SUD) while cameras record every moment. Many of these televised programs show the elegance and grace of a barroom brawl, and one must wonder how much having the television cameras present has changed the dynamics of the intervention session. However, these programs do illustrate different forms of intervention, which is the topic of this chapter.

Surprisingly, health care professionals still have no single definition of intervention. Admittedly, there are benefits to treating the SUDs, providing justification for clinical intervention with those who misuse substances. Researchers have found a 26% reduction in hospitalizations for general health problems, a 25% reduction in the length of hospitalization following admission, a 38% reduction in visits to hospital emergency rooms, and a 14% reduction in physician

¹The material in this chapter is provided for illustrative purposes only. It is not intended for, and should not be used as, a guide to the intervention process.

visits following the cessation of alcohol use, for example (Weiss, 2005). The average monthly medical cost for a person misusing drugs has been estimated at \$750 a month, which is reduced to \$200 a month following treatment, as compared to \$100 a month for a person of the same age who has never misused alcohol or drugs (Rosenbloom, 2000). Given that medical costs may initially rise as a person enters treatment, and with follow-up care, some studies have shown that medical costs may be reduced by almost 50% after treatment for some individuals (Slaymaker, 2013). Further, researchers have found that successful completion of treatment is associated with a significant reduction in suicide attempts and completed suicides (Ilgen, Jain, Lucas, & Moos, 2007).

In spite of these obvious advantages, individuals with alcohol use disorders rarely perceive the need for treatment (Flora, 2005; Wu & Ringwalt, 2005). It must be assumed that the same is true for individuals with other substance use disorders. Thus, some form of intervention is necessary, but the methods for intervention are still in development. In this chapter, the process of Intervention will be reviewed.

A Definition of Intervention

Sadock, Sadock, and Ruiz (2015) suggested that the individual with an alcohol use disorder (the prototypical addiction) must “be brought face-to-face with the reality of the disorder (intervention), be detoxified if needed, and begin rehabilitation” (p. 636). The core concept of intervention is to help the individual with an SUD face the reality of his or her addiction and the harm that it has caused the individual and their family and friends. Intervention may also help the person to realize what harm may come if treatment does not happen (such as medical consequences, family consequences, etc.) (Sadock et al., 2015). However, intervention takes many forms, not just the dramatic events seen on so many television programs. A spouse’s comment that his or her partner is drinking too much is a form of intervention. The physician’s warning that if the person continues to drink or misuse drugs she or he might die is another form of intervention. The supervisor’s warning that the individual seems to have a problem and that he or she should consider going into treatment is yet another form of intervention.

But at what point does feedback from a friend, supervisor, spouse, or the court become a formal intervention project? All forms of intervention begin with the same starting point: *Is it necessary for some form of intervention to be carried out?* If the answer is “no,” then the process stops at that point. If it is agreed that some form of intervention is appropriate, then the decision must be made as to the form of intervention, and who is to participate in that intervention effort. For

the sake of this chapter, **intervention** will be defined as being (a) an organized effort by (b) a person or persons who are part of the person’s environment, (c) to break through the walls of denial and rationalization that surround the addictive behavior(s), which is (d) often supervised by a trained professional, with the goal of obtaining an agreement from the person struggling with an SUD to (e) immediately seek admission to a designated treatment center. In theory, this process is relatively straightforward. The actual application of the intervention process is usually quite difficult.

A Brief History of Intervention

It was once thought that a person with an SUD would not be receptive to efforts to intervene until she or he had “hit bottom.”² Hitting bottom was thought to be necessary for the person to understand that his or her substance use disorder was harming him or her, and that he or she needed to stop misusing chemicals. An unfortunate side effect of this process was that many died before reaching their personal bottom. Others find that they have a successive series of bottoms as they bounce from one situation to another, never accepting the need for them to address their substance use disorder.

Then, Vernon Johnson (1980) suggested a different perspective: He did not believe that the person must hit bottom before being able to accept help with their SUD. Because of the physical, emotional, social, and vocational damage that uncontrolled alcohol use could cause, he advocated early intervention rather than waiting for the person to hit bottom. He suggested that the alcohol-dependent person (with whom he had the most experience) might comprehend the reality of his or her alcohol use disorder if that information was presented in a language that the drinker could understand. Even individuals who were low-functioning (McCrady, 2001), or the individual who was “not in touch with reality” (Johnson, 1980, p. 49) because of his or her substance use was still capable of understanding some portion of the message expressed to him or her, in Johnson’s opinion.

An all too common consequence of intervention efforts is that the person with the SUD will resist efforts from concerned others to guide him or her into a rehabilitation program. To help family and friends address this apparent misperception, a small industry emerged in the 1980s and 1990s in which trained, semi-trained, self-trained, and untrained individuals offered to guide an intervention project. Such intervention projects even became the focus of

²“Hitting bottom” is a term loosely defined as the point where the substance misuser has to admit to total, absolute defeat in life because of his or her SUD.

prime-time television programs. The well-intentioned goal of these projects was to convince a person with an SUD to agree to immediately enter treatment. Having the person simply promise not to drink or use drugs again was not perceived as sufficient, as it was known that individuals with SUDs would often make such promises only to break them the next day. The goal was for the individual to agree to and then enter treatment, and such intervention projects have become enshrined in clinical lore as both useful and often necessary.

Characteristics of the Intervention Process

The characteristics of the intervention process depend, to a large degree, on the setting and the individual(s) involved.

Physician-Based Brief Intervention

One form of intervention is the brief alcohol intervention approach used by many physicians. A physician in the consultation room who informs a patient that if he or she should continue to misuse chemicals, he or she will probably not live another 5 years, and that the physician could recommend some good treatment programs might be said to have attempted to intervene. A brief intervention discussion between a physician and a patient in the emergency room has been found to result in a significant reduction in later alcohol use (SBIRT Research Collaborative Group, 2007). Screening, brief intervention, and referral to treatment (SBIRT) is being implemented into health records systems in our country (Press et al., 2016), and is being used in the ER, primary care, and many other medical settings, and thus appears to be here to stay. Unfortunately, the brief intervention interview with a physician failed to demonstrate a significantly greater reduction in harmful drinking as compared with simply handing the patient a leaflet about the dangers of drinking or a 5-minute session about lifestyle changes (Kaner et al., 2013). Meta-analytic findings suggest that use of SBIRT does not make it more likely that patients will follow through with the recommended services (Glass et al., 2016). These findings cast doubt on the effectiveness of brief physician intervention, and further research into this topic is necessary.

Informal Interventions

The intervention process can take many forms. A spouse who says, "if you don't stop using [X], I'm leaving!" might be said to have attempted an intervention. A friend who expresses concern about his friend's substance use, how much it scares him to see his friend following the same road that he was once following, and how much he would like to see his

friend enter treatment and stop misusing drugs, could also be said to have attempted an informal intervention project.

A supervisor or employer, if asked to participate in an intervention project, might assert that one stipulation of continued employment is that the designated individual take part in a random drug toxicology testing program, and that evidence of illicit drug use or failure to obtain a physician's excuse for taking time off from work for illness will result in the person losing their job. This is a semi-formal intervention project because specific sanctions for noncompliance are identified. Legal intervention projects, which will be discussed later in this chapter, are more formal.

The Mechanics of Intervention

The goal of the intervention project is to assist a given individual in making the decision to stop using alcohol and/or drugs. If informal discussions (outlined earlier in this chapter) have failed to assist the designated individual in making the desired behavior change, a more formal intervention process, usually but not automatically involving family members, might be appropriate. When the decision is reached to attempt a formal intervention meeting, one or more practice sessions should be set up with the individual who will be the chairperson for the meeting. This principle reflects a cornerstone of the intervention process: It is planned in advance. During the planning session(s), the most probable objections and the most appropriate response(s) are discussed. The hoped-for outcome of the intervention project should be discussed, and participants should agree on the specific desired outcome in advance.

The coordinator of the intervention meeting should emphasize that the purpose of the meeting is to allow participants to express their concerns for the designated individual and their desire that the individual enter a rehabilitation program, rather than to allow them to voice their anger about past transgressions (Flora, 2005). Decisions about the proper response to the probable objections and the identification of a specific agency to refer that individual to should be resolved *before* the start of the intervention project.

Paradoxically, by the time intervention projects are being considered, addicted individuals will rarely deny the reality of their substance use disorder, although this might not be true if they believe that the information will be used against them in criminal proceedings (Fletcher, 2013). Individuals with SUDs are usually well aware of their substance use problems, even if they will allow this awareness into their conscious mind only on rare occasions. When confronted, however, many individuals attempt to deflect confrontation with the observation that their substance use is only hurting them, not other family members (Flora, 2005). To break through such rationalizations, the designated individual is confronted by persons

(family members, coworkers, etc.) whose lives have been affected by the individual's SUD. Comments such as "I saw you taking OxyContin from your grandmother's medicine bottle a week before she died of cancer" provide the specific data and demonstrate how the addict's behavior has affected others.

The intervention project is carried out with the goal of having the client agree to enter treatment immediately. If the client admits that perhaps his or her SUD has affected others, and agrees to enter treatment, he or she is then immediately escorted to the treatment center admissions office by family members. When intervention is attempted, the persons doing the intervention should have specific referrals in place. The identified patient has the right to refuse to enter treatment. In such cases, those who participate in the intervention project should have identified sanctions ready to put into place.

These sanctions are not to be viewed as empty threats but rather as the first steps in the process of **detachment**. Through the process of detachment, the person imposing the sanction is saying that he or she will no longer be part of supporting the individual's addiction. Thus, a sister might say, "While you have the right to keep misusing chemicals, you are no longer welcome at my home until you have successfully completed a treatment program." The parents in this hypothetical example might affirm the same decision. A physician might say, "In this case, I can no longer in good conscience continue to prescribe [name of specific medication(s)] to you. The risk of a fatal interaction between the medications that I prescribe and the drugs that you take is too great." A family member might inform the person with the SUD: "You are no longer welcome in my home until you have completed treatment and remain abstinent for a full year." Then these sanctions need to be maintained.

Sometimes, the identified family member will offer vague assurances that he or she will seek assistance, which is used in the service of denial, protecting the substance use disorder. "Yes, I know, you're right," the individual might say. "It's late. I'll call the treatment center tomorrow." However, "tomorrow" never seems to arrive, and the individual offers a thousand and one reasons why they could not enter treatment today, or enter the specified treatment center. "I can't afford to enter treatment! I have bills to pay and need to go to work!" is a common objection offered by the person struggling with the SUD as a reason why he or she cannot possibly enter a rehabilitation program at this time. Such objections might be sincere, but they also deny the reality of the person's SUD. Bills might have been left unpaid, or only partially paid, but the person has always found the money to pay for the alcohol or drugs.

On occasion, intervention efforts will be countered with an effort on the client's part to give the impression of compliance without acceptance of the need to fully enter the treatment process. The family intervention project had required

that they enter treatment. Nobody said anything about the designated person *finishing* it, right? They offer a thousand reasons why they could not complete treatment: "I had to leave . . . they kept stuffing this 'God' crap down my throat!!!" is a common excuse. The reality may very well be that the designated family member heard the word "God" twice in one evening, but as rationalizations go, you have to work with what you have, and this is a good one. Individuals have been known to drive to a treatment center, sit in the parking lot, then after a few hours drive home to say to the family, "I went there and they didn't admit me." By this subtle manipulation of the facts, the person with the SUD implies that she or he did not really need treatment. To avoid such manipulation, designated family members should accompany the addicted member to the treatment center and participate in the admissions interview so that the counselor has an honest overview of the identified patient's substance use disorder and its impact on others.

The identified person will often exploit indecision in the service of his or her SUD to avoid a referral to treatment entirely. Promises will be made and later broken, but by then the unified front by those involved in the intervention project will have been shattered by the demands of each individual's life. Clients have been known to make promises for a lesser sanction, such as going to an outpatient treatment program rather than an inpatient rehabilitation facility, knowing that after a time the family's resolve will weaken and they can drop out of treatment.

Although the intervention process has been in use for more than a generation, more is research needed to support the effectiveness of the programs that have been developed. A recent push for collaboration between treatment professionals and families for intervention efforts (Morgan & Lizke, 2013) as well as continued integration of intervention into medical settings (Press et al., 2016) make this an important area for further study, as it is possible that some families will benefit more from intervention efforts, while others might suffer great harm from the same process. In a very real sense, the intervention process might be said to be the clinical application of a theory that has not been adequately tested to identify either the optimal or minimal conditions where it might be applicable.

The Ethics of Intervention³

The process of intervention is fraught with ethical dilemmas (Scott, 2000). For example, it is based on the assumption

³Persons planning on an intervention process are advised to consult with an attorney as to the specific laws that apply in their geographic location, and what they can or cannot do to carry out the intervention process.

that, through treatment, the person misusing substances can be saved from the negative consequences of the SUD. Further, the “judgement that a person constitutes a sufficiently significant danger to himself or others that some intervention is justified is often highly speculative” (Kleinig, 2004, p. 381). Thus, the need for an intervention must be firmly established and documented. The participant(s) need to carry out an honest, thoughtful review of the benefits and possible consequences of the intervention process, documenting that such a review did take place and what was assessed (Kleinig, 2004).

Another ethical concern is whether the designated individual wishes to participate in the intervention project. The person with the SUD must not be physically restrained, for example, except in cases where there is a danger to self or others.⁴ If the designated individual should express a desire to leave, she or he should be allowed to do so. The designated person is free to leave the intervention program any time, with the exception of when they present a danger to self or others. When the individual is not given any choice to participate in treatment and he or she has not committed a crime, this can be seen as a violation of one’s human rights (Carter & Hall, 2013).

Another ethical concern is whether *informed consent* is a necessary component of the intervention project (Kleinig, 2004). Years ago, the simple authoritative assertion of a health care professional that an intervention program was necessary was sufficient. The courts now hold that the professional must offer informed consent (and document that this was offered) before the client is introduced to the intervention process (Kleinig, 2004). During the intervention process, personal information about the client, or their behavior, might be revealed to other persons who were unaware of these facts. Data privacy is of special importance in hospitals, where persons might be exposed to information about the patient’s substance use disorder in spite of the individual’s desire to keep such information private.

A point of law holds that a patient has the right to refuse any recommended treatment. However, there are exceptions to this rule.⁵ Kleinig (2004) suggested that one such exception is when harm to one person will occur because of the SUD of another person. Because a mother’s cocaine use might harm the fetus, the courts in many different states have remanded many pregnant women into treatment on the GROUNDS that the mother’s continued substance use might harm the fetus (Carter & Hall, 2013; Kleinig, 2004).

The potential conflict of interest must be assessed, especially if the substance rehabilitation professional should refer the client only to him or herself, or to a facility where he or she works (Fals-Stewart, O’Farrell, & Birchler, 2003; Fletcher, 2013). Care must be taken by the substance rehabilitation professional to ensure that she or he has no vested economic interest in where the client goes to treatment. Ideally, the client should be offered a number of treatment options, although in reality, economic and geographic limitations might reduce the options available to the client. Finally, the counselor’s qualifications, and his or her adherence to professional codes of ethics also need to be considered when planning an intervention project (Carter & Hall, 2013; Kleinig, 2004). Obviously, legal counsel is necessary to help the substance rehabilitation professional through the quagmire that surrounds her or him, to avoid violating state or federal laws (Scott, 2000).

Some Common Forms of Intervention

Family Intervention Projects

There are a number of family intervention project models, the most familiar of which is the format advocated by Johnson (1986). Collectively, these family intervention efforts are second only to legal pressure to force the individual into treatment (O’Farrell & Fals-Stewart, 2008). However, it should be recognized that the person who is the center of the intervention project is unlikely to be enthusiastic about the process, and there is a danger for serious damage to familial relationships as a result of family intervention programs (Blume, 2005; Flora, 2005). This danger is increased if the intervention project is poorly planned or executed. While the goal is that the intervention project be carried out without malice and in a nonjudgmental manner (Fals-Stewart et al., 2003; Sadock, et al., 2015), many family members will view the intervention project as a time to voice resentments about the individual’s SUD or past behaviors, increasing the danger of a negative outcome. It must be recognized that family intervention sessions are “emotional powder kegs that can go horribly wrong” (Flora, 2005, p. 41). What follows is a brief summary of two of the more common family intervention models.

THE JOHNSON MODEL

This is the model most often associated with the word *intervention*, and its original form was advanced by Johnson (1986). This form of intervention is portrayed in many popular books, articles, and the occasional prime-time television

⁴In which case the police should be called.

⁵Thus, the recommendation that the substance rehabilitation professional seek legal counsel as to the laws that apply in her or his state before attempting an intervention.

program, usually in a positive light. Johnson model intervention projects usually involve three or four educational or rehearsal sessions before the actual intervention effort, to prepare family members, friends, or coworkers for the actual intervention session. Those persons who are either actively abusing alcohol or illicit drugs, or who refuse to participate in the intervention project, should not be invited (O'Farrell & Fals-Stewart, 2008).

During the pre-effort training sessions, participants are taught about the disease model of addictions, reducing the potential for anger or malice as the participants learn that the affected person suffers from a disease and is not intentionally being mean or unsupportive. Family members are encouraged to bring written notes to the intervention session with them. Such notes should be very specific as to dates, times, and the client's behaviors that resulted in that person's decision to be part of the intervention project. Statements such as "you often come home drunk" should be replaced with specific comments such as "Last week you came home intoxicated on Monday, Wednesday, Thursday, and Saturday night!"

Role-play simulations are also carried out to prepare family members for possible scenarios that might emerge during the actual intervention session. If, for example, the person struggling with an SUD should claim not to have driven while under the influence after going to the bar because "Mark drove me," a family member should check with Mark (if he is not a participant) to see whether this excuse is valid. Other possible scenarios to be addressed include what to do if the affected family member should become angry, attempt to leave, or attempt to manipulate family members into disagreement. During these pre-effort sessions, family members will discuss the goal of the intervention project (usually to secure a commitment to immediately enter treatment). If successful, the participants will have prearranged admission to a treatment facility.

When all is ready, the affected family member is either invited or escorted to the intervention effort session. Such sessions often have all the elegance and style of a hanging in the days of the wild west, and as noted there is the danger for lifelong damage to familial relationships even in the best of intervention efforts. Further, in spite of the intentions of participants, Johnson (1986) model intervention programs result in a commitment to enter treatment only in approximately 30% of cases (Miller & White, 2007; O'Farrell & Fals-Stewart, 2008).

THE ARISE MODEL⁶

This is a three-stage model of intervention in which the level of pressure applied by the family to encourage the affected

member to enter treatment is gradually increased (Landau & Garret, 2006). This model is based on a graduated series of contact sessions with the patient over a period of time, with the goal of securing the addicted person's entry into treatment. The first stage is usually telephone contact with the client, followed by a family therapy session to explore the problem and its ramifications. In stage two, the client is invited to attend a family therapy session, and the entire family discusses options that they see available to them at that time. In the third stage, if the individual does not enter treatment within a designated period of time, a more confrontational intervention session comparable to the Johnson model in many respects is then carried out. In this manner, the client is only exposed to strong levels of confrontation if he or she should fail to respond to more gentle feedback from family members about how the individual's substance use disorder has affected them.

Intervention by the Legal System

Individuals who participate in court-mandated treatment arrive at this point through a variety of avenues. Some have been convicted of driving a motor vehicle while under the influence of alcohol or drugs (a "DWI," as it is called in some states⁷). Others may have been arrested for possession of illicit drugs, or for any of a wide range of substance-related legal offenses. In theory, the individual retains the right to choose incarceration over treatment (Leamon, Wright, & Myrick, 2008). Essentially, the individual is placed into an either/or situation: Either the client successfully completes treatment or he or she will go to jail. This is called **contingency management** (Morgan, 2006). Individuals who enter a rehabilitation facility under such situations are said to demonstrate controlled motivation (Wild, Cunningham, & Hobdon, 1998). Unfortunately, court-mandated treatment is rarely viewed as an opportunity for growth, and is usually viewed as a punitive response by the legal system for past behavior(s) by the individual (Dill & Wells-Parker, 2006). Those who have been mandated to treatment have mixed opinions about the usefulness of being ordered to treatment (Kras, 2013), yet there is a need to continue to consider mandated treatment options for public safety reasons (Miller & Miller, 2016).

Court-mandated treatment reflects the theory that the individual might benefit from external motivation during the early stages of recovery from an SUD (DiClemente, Bellino, & Neavins, 1999; Satel, 2000; Satel & Farabee, 2005). It is hoped that eventually internal motivation might develop, and the individual will apply themselves to the treatment

⁶Which stands for A Relational Intervention Sequence for Engagement.

⁷In other states, it is called an "OWI," or "operating a motor vehicle while under the influence of intoxicants."

process. There is mixed evidence suggesting that court-mandated clients work harder on treatment goals than voluntary patients, and are also less likely to prematurely leave treatment if they are there because of an agreement with the court. This process offers the additional advantage that the very nature of the circumstances surrounding admission makes it quite difficult for the client to deny that they have a problem with chemicals!

Court-mandated clients have been found to have experienced fewer negative consequences from their substance use than do clients without legal pressure (Kelly, Finney, & Moos, 2006). At first this would seem counterintuitive, until one considers that the voluntary client is more likely to be older and to have experienced some of the adverse physical or social consequences of his or her SUD. The court-mandated client has also been found to be as likely to benefit from treatment as traditional patients (Kelly et al., 2005; Satel & Farabee, 2005). Further, there is evidence that those persons who seek treatment at the insistence of the court system may remain in treatment for a longer period of time than traditional clients, and are less likely to reoffend following discharge from treatment (Satel & Farabee, 2005).

In spite of the obvious benefits of court-mandated treatment, there are also some problems with this form of treatment. First, many insurance companies are, by law, able to refuse payment for court-mandated treatment (Dill & Wells-Parker, 2006). Court-mandated treatment is not a guarantee of long-term abstinence, since long-term abstinence rates for those who complete treatment at the invitation of the courts appears at best to be the same as for voluntary patients (Leamon et al., 2008). Further, some clinicians view court-mandated treatment as being coercive and feel that the outcome of this process is coerced abstinence (Jaffe & Anthony, 2005; Szasz, 2009). Treatment by court order places special requirements on the treatment center.⁸ Such treatment also raises interesting questions about the relationship between the law and the rehabilitation industry: If, as the medical model asserts, alcoholism is a disease, then how can the courts order it cured? Thus, there is some disagreement among treatment professionals as to the value of court-mandated treatment.

Drug Court

The *drug court* concept was first tried by the Miami-Dade County, Florida, in 1989 (Speck, Connor, Hartig, Cunningham, & Fleming, 2008), and since then over 2,000 similar

programs have been instituted in 1,100 counties across the United States (Speck et al., 2008). The goal of drug court is to:

quickly identify substance abusing offenders and place them under strict court monitoring and community supervision, coupled with effective, long-term treatment services [during which] the drug court participant undergoes an intense regimen of substance abuse and mental health treatment, case management, drug testing, and probation supervision while reporting to regularly scheduled status hearings before a judge with specialized expertise in the drug court model.

*Huddleston, Freeman-Wilson, and Boone
(2004, p. 1)*

Accountability is the core concept of the drug court (Speck et al., 2008). Such programs are most effective for first-time, nonviolent offenders with the goal of avoiding the “revolving door” cycle of repeat offenses (Goldkamp, White, & Robinson, 2002). Drug court programs should (Work Group on Substance Use Disorders, 2007):

1. assess the individual's need for treatment
2. identify the proper level of treatment for the client
3. identify the treatment facility best suited to the client
4. monitor client adherence to treatment through therapist reports
5. administer periodic urine toxicology tests
6. provide for a reduction in legal charges if the client completes the program
7. provide for aftercare groups, etc.

The drug court program is comprised of three stages (Speck et al., 2008): Stage I: Detoxification, which is usually completed within 14 days unless the individual was abusing drugs with longer half-lives, or has relapsed during the detoxification period. During this phase, there is an intensive schedule of individual and group therapy sessions, as well as regular court sessions, that the client must follow. Readiness to move on to Stage 2 is dependent on staff assessment of the individual's progress and a history of seven consecutive “clean” urine toxicology tests (Speck et al., 2008). Once this transition is achieved, the client moves into Stage 2: Stabilization. This stage can last from 16 to 52 weeks, depending on the needs of the individual (Speck et al., 2008). The individual is expected to follow a very intense schedule of individual and group therapy sessions, community support group meetings, and maintain frequent contact with the court. Urine toxicology testing during this stage is expected to show no evidence of alcohol or drug use. If the individual should relapse, staff have the option of referring the client back to Stage 1, or simply starting the client over at the start of Stage 2.

⁸For example, the treatment center might be expected to *immediately* notify the authorities should a client leave treatment against staff advice.

When deemed ready, the client moves on to Stage 3: Aftercare, which lasts from 8 to 9 months. Clients continue the regimen of individual and group therapy appointments, but also start to prepare for self-directed recovery and living (Speck et al., 2008). This might require that the client participate in literacy training, earn long-neglected a high school equivalency or GED diploma, and start to train for employment in the client's chosen field. The client is still expected to abstain from alcohol or illicit drug use, and if they should relapse the staff has the option of placing them in an earlier stage to relearn necessary skills from that stage.

There has been some dispute concerning the effectiveness of the drug court programs, which are both labor- and time-intensive. Reuter and Pollack (2006) suggested that these programs are both cost-effective and have lower recidivism rates. For example, it was estimated that New York State saved \$250 million in one year through its drug court programs, while in St. Louis, Missouri, it was found that for every \$1 invested in drug court, there was a savings of \$6.32 in reduced welfare, medical, and law-enforcement expenses (Taylor, 2004). In contrast to these claims, Eckholm (2008) suggested that drug courts only reduce recidivism 8–10%, a figure that is only slightly higher than the figure of 13% offered by Rempel (2005). Speck and colleagues (2008) offered a more optimistic recidivism rate of 17%, as opposed to 66% for those who are simply incarcerated.

While such data is very promising, there have been few well-designed studies into the effectiveness of drug court programs, as the very nature of the population served would make such research difficult, if not impossible (Rempel, 2005). Those studies that have been carried out have been classified as unreliable at best, because (a) the very people who design a local drug court program are the ones who also design and carry out tests of its effectiveness; (b) the drug courts “cherry pick” (Drug Policy Alliance, 2011, p. 2; Justice Policy Institute, 2011) the clients admitted to the program, typically those convicted of petty crimes or low-level drug-use law violations; (3) the short-term periods of incarceration used for rules infractions often collectively add up to *more* time than if the individual had served their original sentence; and (4) the financial costs of these programs is often underestimated (Drug Policy Alliance, 2011). Newer research by Contrino, Nochajski, Farrell, and Logsdon (2016) found that those attending a drug court program remained in the program because of the positive improvements in their lives, although acknowledging as well that avoidance of jail was why they entered in the first place, which would still be a factor in completion.

Nationally, various drug court programs report successful graduation rates of 30–70%, and in many programs there is a tendency for increased recidivism following discharge from

the program for any reason (Drug Policy Alliance, 2011). Further, the core concept of the drug court program forces the judicial system to adopt a punitive stance toward addiction, which is the antithesis of the disease model. While many participants are referred to either outpatient or inpatient rehabilitation programs, access to such programs is often limited.

One problem with the drug court concept is that it is based on the theory that the substance treatment programs that the clients are referred to are effective. This is at best an unsupported assumption, since it is quite challenging to determine what counts as effectiveness, let alone effectiveness of individual programs. Further, the drug courts place an additional demand on the already limited number of treatment beds through mandated treatment requirements. Participation in a drug court program requires an admission of guilt on the part of the client, and while the charges are dropped when the individual successfully completes the program, many potential participants opt for the possibility of being found not guilty (McPherson, Yudko, Afsarifar, & Freitas, 2009).

Finally, the issue of the individual's motivation to participate in a drug court program must be considered. Some drug courts have admitted individuals who are not addicted to drugs, but who wish to avoid prison for the sale of such compounds. Since these individuals were never addicted to the compounds that they sold, this would inflate the success rate of that drug court program (Eckholm, 2008). Thus, the issue of the drug court movement, its effectiveness, and when the individual should not be referred to a drug court program is quite complicated.

Court-Mandated Involuntary Treatment

In more than 30 states it is possible for a person to be committed to a treatment facility against his or her will. To do this one must prove to the courts that the individual is in imminent danger of harm to self or others (Gendel, 2006). The provisions under which a person might be remanded to treatment vary from state to state, but, in essence, this provision of the law provides for the person to be sent to treatment against his or her will if there is reasonable evidence to believe that he or she is a danger to self or others. While these laws are often utilized to send one person or another to a rehabilitation program, there is little evidence as to the effectiveness of court-mandated involuntary treatment. There is a very real chance that the client will simply comply with treatment expectations to escape the court's supervision as rapidly as possible, without making any permanent changes in his or her substance use behaviors.

It is rare for an individual to request treatment, a phenomenon known as **autonomous motivation** (Wild et al., 1998). It is more common for the individual to admit that she

or he would continue to misuse chemicals if she or he could do so. It is for this reason that external pressure in the form of familial, legal, or professional pressure is utilized to help the person struggling with an SUD see the need for treatment.

Other Forms of Intervention

Morgan (2006) suggested that **contingency management** techniques are often very effective when working with individuals with an SUD. In a sense, contingency management situations are “either/or” forms of external pressure similar to sanctions often utilized by the courts to help an individual find the motivation to enter treatment. A spouse might confront his or her partner with the warning, “If you don’t stop abusing alcohol or drugs, I am filing for a divorce!” If the individual should continue to misuse chemicals, then the partner should follow through with the sanction and file for divorce. A failure to do so means that warnings of further sanctions will be ignored by the person struggling with an SUD, since the partner did not enforce the original sanction.

Thus, a person who had made a request that his or her friend not drink before or while they are playing golf, upon seeing that the friend was drinking a beer, might just turn around and leave. The plea from the drinker that it was “only beer” should be met with the comment, “I said that if you were drinking, or appeared to have been drinking, I would not play golf with you.” The previously stated sanction is then enforced, and should remain in place until the drinker does indeed enter treatment.

Employer-Mandated Treatment

With the advent of workplace urine toxicology testing to reduce employee accidental injuries and use of sick leave, it is not uncommon for people to seek admission to substance rehabilitation programs because their employer threatened to fire them if they did not. Employers justify such behavior on the grounds that employee substance use disorders cost them money. A company with just 500 employees will typically spend \$133,000 in health care costs for alcohol-related problems among employees each year (Brink, 2004). Further, individuals with an alcohol use disorder use more sick days, and are five times as likely to file a worker’s compensation claim as nondrinkers (Brink, 2004). Thus, employers feel justified in guiding employees into treatment or out the front door. Surprisingly, there is little research into whether such employer-mandated treatment is effective, or the conditions under which it is most useful. Individuals often find it more convenient to just quit and look for alternative employment rather than enter treatment as the original employer suggested.

Reactions Against the Concept of Intervention

A common misperception of the intervention-treatment recommendation process is that the individual is sent away to get “fixed.” In reality, intervention is part of the assessment/intervention/treatment continuum, and it involves both the individual with the SUD and the family. It is part of a growth process for all concerned.

While the intervention process might obtain a commitment to enter rehabilitation from the person misusing substances, it is also not uncommon for individuals who are referred to a rehabilitation program to object that “treatment does not work.” This is a myth, although a popular one among those who seek to avoid admission to a substance rehabilitation program. Research has demonstrated that rehabilitation programs are cost-effective.⁹ However, *when* does coercion for a person to enter treatment work, even if that treatment is cost-effective? In his discussion of this topic, Bentall (2009) argued that:

paternalism and coercion could be justified *only* if doctors and other mental health professionals reliably knew what was in their patient’s best interests. However, their track record is appalling.

Bentall (2009, p. 273, italics added)

This is supported by Marano (2012), who observed that confrontational methods such as the Intervention process as practiced in the United States are unique to this country. Such intervention programs imply that those who confront the person with the addiction are somehow morally and psychologically superior to the subject of the intervention (Marano, 2012), an often dubious assumption. Further, while rehabilitation professionals are governed by the principle “first do no harm,” coercion has become such an accepted tool among mental health and medical professionals that it now does not raise ethical questions for those who wield these weapons against individuals who by social standards might have a “problem” (Bentall, 2009).

Chapter Summary

In rare cases, clients will demonstrate autonomous motivation for treatment. However, because of the pharmacological reward potential of the drugs of misuse, most persons struggling with SUDs are not necessarily interested in abstinence

⁹As discussed in Chapter 38.

or recovery. Thus, contingency motivation has been viewed as an appropriate manner to guide the addicted person to rehabilitation. It is hoped that while in treatment, the individual will come to see how her or his life was out of control and centered around continued chemical misuse, in spite of the damage being wrought to both themselves and significant others.

Intervention projects may be informal, as when a physician confronts a patient with the reality that continued substance use will result in a deterioration of health, and ultimately death. Another informal intervention might be seen when a friend sets a limit as to what he or she will tolerate in the relationship, and then when the individual with the SUD continues to engage in substance-related behaviors, enforces sanctions such as ending the friendship. An employer or supervisor might confront an employee with evidence that his or her continued substance use is harming productivity, and that if he or she does not enter treatment and maintain continued abstinence following the completion of rehabilitation,

the employee will be fired. Formal intervention projects involve family members and friends meeting with the identified individuals, confronting them with evidence of how their SUD is hurting both themselves and others, and attempting to obtain a commitment from the identified individuals to immediately enter treatment. If the client agrees, then appointed family members will escort the individual to an identified treatment center, and participate in the admissions interview. If the client should refuse, then previously identified sanctions are to be employed to help family members and friends detach from the person with the SUD and his or her behavior.

The rights of the individual who is the focus of the intervention process are discussed in this chapter, as is the fact that the identified patient has the right to leave the intervention project should he or she wish to do so. Employer- and court-mandated interventions are discussed, as is the fact that the effectiveness of such incentives for treatment remain unsupported.



CHAPTER 30

Treatment Settings

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 30.1** Define and identify various types of outpatient rehabilitation programs
- 30.2** Understand the advantages and disadvantages of outpatient rehabilitation programs
- 30.3** Define and identify various types of inpatient rehabilitation programs
- 30.4** Understand the advantages and disadvantages of inpatient rehabilitation programs
- 30.5** Define and identify various types of aftercare programs

Introduction

In Chapter 28, we reviewed some of the many issues that must be addressed during the screening and assessment process. However, there is a question that is rarely asked: Is treatment necessary? After all, Willenbring (2010) suggested that three-fourths of those people with an alcohol use disorder reduce or stop drinking entirely without professional treatment or involvement in a 12-step support group. However, if the individual has failed in an attempt to quit the misuse of chemicals, or if the disorder is causing severe interpersonal or medical problems, a referral to a rehabilitation program is strongly indicated. Depending on the client's assessed need for a specific level of care, the treatment process might take place on either an outpatient or an inpatient basis. There is a great deal of debate within the professional community as to the relative merits of each treatment setting, but the emerging consensus is that each offers advantages and disadvantages for both the rehabilitation center staff and the client. The advantages of rehabilitation are clear: Individuals who were involved in a treatment program or 12-step program were more likely to be abstinent 16 years after they entered rehabilitation (Moos & Moos, 2006a, 2006b). In this chapter, we will briefly review the different settings where the client's substance use disorder might be addressed.

Detox Programs

The first question that must be addressed by a medical professional is whether medically supervised "detoxification" ("detox") is necessary. If it is deemed necessary for the individual to go through a detoxification regimen, the decision must be made as to whether this can be safely carried out on an outpatient basis or if it should be carried out within a medical facility. Detox programs will be discussed in the next chapter, but it is necessary to point out that a detox

program is not the same as a substance use treatment. Detox is *not* a form of treatment, but the supervising staff can make referrals to rehabilitation programs while the person is in the process of being withdrawn from the drug(s) in his or her system. The treatment referral might be to either an outpatient or an inpatient rehabilitation program, some of the varieties of which are discussed below.

An Introduction to Outpatient Treatment

Outpatient Treatment: A Working Definition

The **outpatient substance rehabilitation program** might best be defined as (a) a formal treatment program involving one or more rehabilitation professionals, (b) designed to help the person with an SUD develop and maintain a recovery program, (c) which will utilize a variety of treatment approaches (psycho-educational, family and marital therapies, individual and group therapy formats), which is (d) designed to do so on an outpatient basis.

Outpatient treatment programs are quite popular, and it has been estimated that 85% of all patients who participate in a substance rehabilitation program will initially be treated on an outpatient basis (Tinsley, Finlayson, & Morse, 1998). While many individuals might come to terms with their substance use disorder through outpatient treatment, such programs might also serve as a transitional, or step-down, stage for persons who originally were in an inpatient program and for whom a less intensive form of support is thought appropriate before they attempt self-directed recovery (Work Group on Substance Use Disorders, 2007).

Components of Outpatient Treatment

Outpatient treatment programs will often utilize both individual and group therapy formats to help the client address his or her SUD, with ancillary treatment services such as assertiveness training, marital and family therapy, vocational counseling, etc. Most outpatient treatment programs follow a 12-step format, and clients are expected to attend regular self-help group meetings on their own as part of their rehabilitation plan. The person who coordinates this program is a certified chemical dependency counselor or mental health professional who specializes in the treatment of the addictive disorders.

A formal treatment plan is established at the beginning of treatment, with review sessions scheduled on a regular basis to monitor the client's progress toward mutually

agreed-upon goals. Psycho-educational lectures and bibliotherapy¹ are also often utilized in outpatient rehabilitation programs to help the client recognize the consequences of his or her SUD if it is not arrested. Such programs might also have a "family night" component held either once a week or once a month, where family members might ask questions or express concerns about the client's progress, the nature of the addictions, etc. Such family nights should not be interpreted as "family therapy," which is a more intensive process (Fletcher, 2013).

Abstinence from alcohol and illicit drugs is not only expected, but is usually a prerequisite for continued participation in outpatient treatment. Appropriate pharmaceutical supports² prescribed by a physician are often called upon, and progress is confirmed through the client's self-report, collateral information, alcohol breath testing, and urine toxicology testing. If the client should relapse, this is also addressed on an outpatient basis unless it becomes apparent that the client is unable or unwilling to abstain from chemicals while in an outpatient treatment program. In this case, a referral to a more intensive level of treatment would be indicated.

Although intuitively one would expect that individuals referred to outpatient rehabilitation programs would be unlikely to discontinue treatment since such programs are inherently less intrusive than residential programs, research has found just the opposite: Outpatient rehabilitation programs experience high dropout rates, and many of those who do enter outpatient rehabilitation programs eventually are referred to a residential treatment center, where the likelihood of completing treatment is almost three times higher (Stahler, Mennis, & DuCette, 2016).

Varieties of Outpatient Rehabilitation Programs

There are a number of different outpatient treatment formats, and client referral to one form of treatment or another is dependent on the available resources and the client's assessed needs for a specific level of care. Perhaps the least restrictive form of treatment is the DWI school.

DWI SCHOOL³

These programs (also sometimes called DUI school, drunk driving education, or possibly alcohol education program) utilize a psycho-educational approach, and are usually limited

¹ Assigned readings of specified material to assist in the rehabilitation process.

² Discussed in Chapter 33.

³ Which is short for "driving while under the Influence of mood altering chemicals." In some states this is called an "OWI," or operating a motor vehicle While under the Influence of intoxicants.

to the first-time offender who is assumed to have made a mistake by unintentionally driving a motor vehicle under the influence of alcohol or other mood-altering chemicals.⁴ Individuals referred to a DWI school are not, in the opinion of the assessor, addicted to alcohol or drugs. The DWI school format usually involves 8–12 hours of educational lectures, as well as individual and group therapy sessions to help the individual better understand the dangers associated with operating a motor vehicle while under the influence of chemicals. There are a variety of different programs, and states vary on whether such programs are used as penalties.

INDIVIDUAL REHABILITATION COUNSELING

Depending on the individual's needs and the severity of his or her substance use disorder, he or she might be seen by an addictions counselor or professional-level mental health therapist on a one-on-one basis. Such treatment approaches are usually restricted to motivated clients who are willing to engage in inter-session assigned projects (assigned reading, for example) and utilize existing support services (12-step groups, etc.). The treatment orientation of the addictions counselor will depend on her or his training and experience, but might include motivational interviewing, cognitive behavioral, and/or 12-step-oriented techniques.

SHORT-TERM OUTPATIENT PROGRAMS

These programs are usually time-limited, and are aimed at helping those persons with a mild to moderate SUD achieve abstinence. Short-term outpatient programs utilize a blend of individual and group therapy formats, with the client being seen one or two times a week. In addition, participants might be expected to attend at least one self-help group meeting a week, are assigned material to read before the next individual or group session, and are expected to meet with their case manager at least once a week for between 1 and 2 months.

INTENSIVE SHORT-TERM OUTPATIENT PROGRAMS

These programs are called by a variety of names, including “partial hospitalization,” or “evening” or “day treatment” programs (Work Group on Substance Use Disorders, 2007). These programs might serve either as a primary treatment intervention for the client or as a step-down level of treatment for patients who have completed a residential treatment program (Weiss, Potter, & Iannucci, 2008; Work Group on Substance Use Disorders, 2007). Clients are usually seen four or five times a week. Treatment is carried out through a blend of individual and group therapy formats, and such programs last for up to six months. Ancillary services such as family or marital counseling are utilized as necessary, and

clients are expected to participate in a community support group⁵ meeting at least once a week.

INTENSIVE LONG-TERM OUTPATIENT TREATMENT

These programs are usually open-ended, and are designed for the individual whose SUD has been assessed to be moderate to severe in intensity. Individuals referred to these programs have usually been unable to achieve lasting abstinence either on their own or after completion of less intensive treatment programs. Clients are seen for a blend of individual and group therapy sessions, and are seen for 3–5 days or nights a week for between 12 and 18 months. Ancillary services such as vocational counseling, individual psychotherapy, and marriage and family therapy are offered as needed. The participant is expected to attend at least one community support group meeting a week.

Advantages of Outpatient Rehabilitation

Outpatient treatment programs are quite popular. There are a number of reasons for this popularity, not the least of which is that they are far less expensive than residential treatment programs. It has been estimated that outpatient treatment programs cost between \$5,000 and 10,000 for 3 months (“Understanding the cost of rehab,” 2017) as opposed to \$6,000 on the low end (“Understanding the cost of rehab,” 2017) to \$60,000 for a 30-day residential treatment program at the high end (Fletcher, 2013, p. 104). Outpatient treatment programs also minimize the need to remove the individual from his or her daily environment, allowing him or her full participation in normal family life, continued employment, etc. Such programs also avoid the need for a reorientation period after the individual graduates from the treatment program. Further, such programs offer some degree of flexibility, allowing alterations to accommodate the client's work schedule or family emergencies, as needed. A mixed blessing is that outpatient rehabilitation programs do not remove the individual from his or her environment, forcing the individual to confront drug-use cues within the context where he or she engaged in alcohol or drug misuse in the first place. This might allow the client to practice recovery skills learned while in treatment while still living in his or her home, which can result in the client achieving a sense of mastery. This might also result in the client's relapse.

⁵There was a time when Alcoholics Anonymous (AA) or Narcotics Anonymous (NA) were only the community support groups available to the recovering person. There have been a number of faith-based and nontraditional community support groups founded, providing some alternatives to either AA or NA. These groups will be discussed in Chapter 35.

⁴One fact that many people do not understand is that it is possible to be charged with driving while under the influence (DWI) while taking prescribed medications if those chemicals are mood-altering compounds.

Disadvantages of Outpatient Treatment Programs

This review of outpatient treatment programs is not to suggest that such programs are a panacea, nor are they the ultimate solution to the problem of substance use disorders. Graduates of outpatient treatment programs are as likely to relapse as are those who successfully complete a residential treatment program (Ritvo, Martin, & Fehling, 2015). This is not to imply that these programs are equally effective (or ineffective) as residential treatment. Outpatient programs tend to work with a different client than do residential facilities. This fact makes comparison between the two types of programs difficult.

While residential treatment programs are generally far more expensive than outpatient treatment, because of insurance company co-pay requirements it is possible that residential treatment will actually cost the individual less out of pocket for residential as opposed to outpatient treatment (Fletcher, 2013). Indeed, the coverage for treatment can be quite different across health insurance policies, with the possibility of some not covering outpatient treatment at all.

Another disadvantage of outpatient treatment is that such programs do not offer the same degree of structure and support inherent in a residential treatment setting. Family members might be reluctant to report substance use relapses or inappropriate behaviors on the part of the client, and the individual might have a limited abstinence-based support system. Such problems indicate that outpatient treatment programs are of limited applicability for clients who require a great degree of support during the earliest stages of recovery. Clients are often left in the position of having to endure strong cravings for chemicals in the very environment in which they were misusing them. Exposure to drug-use cues may certainly contribute to the high relapse rate seen in graduates of such programs. If the client does relapse, she or he will need to be reassessed to determine the proper level of treatment. These problem areas are sufficient to suggest that outpatient treatment is not the ultimate answer to substance use disorders and that residential treatment might be necessary.

Introduction to Residential Treatment Programs

Definition of Inpatient Treatment

Surprisingly, there is no standard definition of inpatient (or, as it is often called, “residential”) **treatment** (Weiss & Dreifuss, 2015), as this term can describe a variety of settings and programs. Residential treatment programs provide a 24-hour treatment milieu, with staff members on duty

24 hours a day. However, staffing levels vary from one program to the next. Some residential treatment programs are poorly equipped to meet the needs of patients who require acute medical care, and they will refer these individuals to other facilities. Other programs, usually based in a hospital setting, treat the person’s medical problems in-house (Weiss & Dreifuss, 2015). Despite the differences, residential treatment programs all share the characteristic of offering a more intensive focus on the individual’s recovery from the SUDs than outpatient treatment programs (Work Group on Substance Use Disorders, 2007). These programs are, broadly speaking, effective in working with the resistant, suicidal, or homicidal clients, or clients who are unable to abstain in the less restrictive outpatient treatment programs (Work Group on Substance Use Disorders, 2007), depending, of course, on the resources of the particular residential program.

Most residential treatment programs have a strong 12-step group orientation, with clients being expected to attend multiple 12-step meetings during the week. Some programs carry out all treatment activities in a group setting, while other programs allow for ancillary appointments with psychologists, social workers, dietary therapists, etc. as indicated (Fletcher, 2013). Barriers to recovery are identified through meetings with treatment staff, including an assessment of the client’s support system, level of motivation, and past treatment history, with appropriate interventions being designed to help the individual address problem areas in his or her life.

The decision to utilize inpatient treatment as opposed to an outpatient treatment program is based on the assessed need for a specific level of care.⁶ Such programs might be offered, for example, at a general hospital, a freestanding facility, or in a therapeutic community setting (Weiss & Dreifuss, 2015).

Hospital-Based Residential Treatment

Hospital-based rehabilitation programs offer a range of services, including (but not limited to) medical stabilization for ongoing (often untreated) medical problems; group, individual, marital, and family therapy programs; psychoeducational programs; and social service support as needed (Work Group on Substance Use Disorders, 2007). Clients will also have assigned “homework” projects, and **bibliotherapy**⁷ while in treatment. While many of these programs utilize the “Minnesota Model,”⁸ managed care initiatives have made this less common as insurance companies have demanded shorter

⁶Discussed in Chapter 28.

⁷See Glossary.

⁸Discussed in the next chapter.

stays for clients (Weiss & Dreifuss, 2015). There is usually a strong emphasis on 12-step group participation, and clients are expected either to participate in 12-step group meetings held within the hospital, or they are escorted to community-based 12-step group meetings (Fletcher, 2013).

There is no set duration for residential community treatment, although the goal is to help the client reach a point where she or he can abstain from alcohol or drugs with the support of less restrictive outpatient treatment programs. Funding is always a major consideration, and treatment center staff need to balance the client's needs against available funding from the client's health care provider and the client. These topics will be discussed elsewhere in this text.

Therapeutic Communities

The *therapeutic community* (TC) concept originated in the 1960s as a self-help alternative to traditional treatment programs for drug addiction (De Leon, 2015). The original TCs were marked by harsh ego-stripping confrontation techniques that included 24-hour "marathon" group sessions as well as a "hot seat" in the center of a group circle where a person was expected to sit while group members confronted them with perceived personality flaws. All staff positions were held by former residents, with minimal input from health or mental health professionals. Some TCs expected a lifetime commitment from the client, who was viewed as unable to live independently without substances and therefore had to remain within the therapeutic community.

The TC movement has moved away from these early techniques to become a more generic term for a range of programs that include short term residential, long-term residential and some day treatment programs. Some TCs also have made provisions to work with particular groups, such as with women who have children, or patients with HIV/AIDS (De Leon, 2015). However, all of these modifications of the original therapeutic community program concept retain the core belief that the SUDs reflect the individual as the problem, and the SUD is the symptom of the multiple areas within which the person is deficient (De Leon, 2015). According to this theory, reflections of the individual's dysfunction might be seen in mood disturbances, unrealistic thinking, as well as educational, social, and moral deficits. In response to the arrested development of the person struggling with an SUD, the TC attempts to assist the individual in making a global lifestyle change, allowing life without the substances (De Leon, 2015). Unlike the original therapeutic communities, current TCs prescreen applicants, excluding those persons who have a history of attempted suicide or homicide, attempted arson, or severe uncontrolled psychiatric disorders from admission (De Leon, 2015).

Therapeutic communities are usually freestanding⁹ programs which, although initially quite resistant to the use of 12-step community support groups, have started to integrate these self-help groups into the program (Ringwald, 2002). TCs usually utilize a highly structured daily program that usually starts at 7 a.m. and continues until 11 p.m. This structure, plus the belief that it is the community that is the agent of change or healing, are thought to assist in the desired personality change. In a sense, the TC might be viewed as providing an extended family for the program participant. The TC program format has evolved to the point where it has been integrated into some penal institutions to work with convicted felons who have an SUD, and with persons who have addictions to multiple compounds (De Leon, 2015).

Clients are viewed as passing through three different stages during treatment: (a) compliance, (b) conformity, and (c) making a personal commitment for change (Satel & Farabee, 2005). To assist the individual in moving through these stages, the TC retains a strong emphasis on self-examination as well as public confession of past misbehavior, both within the group and during individual counseling sessions. More advanced clients are presented as role models for initiates, and while there are a small number of professional staff in most modern TCs, it is peer support and appropriate confrontation that are viewed as the main vehicles of change (De Leon, 2015). Participants are expected to carry out assigned work projects, first within the TC itself, and later in the outside community, which is considered a privilege that the program participant earns through his or her progress in the TC program.

De Leon (2015) also suggested a three-stage model for long-term TC programs: (a) orientation/induction, (b) primary treatment, and (c) reentry. During the first phase, orientation/induction, which lasts for approximately the first 60 days, the person is confronted with the tasks of being oriented and assimilated into the program, while staff continue to assess the individual to determine whether participation in the TC is appropriate (De Leon, 2015). The second stage, primary treatment, lasts from the second until the twelfth month, during which time the individual learns to become more autonomous, accept more desirable job assignments within the TC, and begin to teach others (De Leon, 2015). The final stage, reentry, lasts from the thirteenth until the twenty-fourth month and focuses on helping the individual strengthen skills for maintaining abstinence, autonomous decision making, and vocational skills. During this phase, the

⁹Is not associated with a hospital program and is funded either through donations or monies earned by participants who work in various capacities in the community.

individual might find a job outside the TC to both earn a salary and begin the transition to independent living.

Some components of the TC program include tutorial sessions, which include training and educational experiences for the clients (De Leon, 2015). Individual therapy sessions are also held, and a small minority of TCs still hold encounter groups or marathons, which are extended groups aimed at helping individuals resolve life experiences (a history of sexual or physical abuse, for example) that are thought to have contributed to the individual's substance misuse (De Leon, 2015). Unannounced urine toxicology testing is also carried out on a random basis, with decisions concerning the retention of the client, in-house job assignments, or whether to allow the client to progress from one level to the next being made in part on the basis of the results of these tests (De Leon, 2015).

Where the original TCs would only accept self-referrals to the program, estimates are that between one-quarter and two-thirds of program participants are under the supervision of probation or parole agents (De Leon, 2015; Hiller, Knight, Rao, & Simpson, 2002). This distinction may relate to the combining of groups with some statistics, as most TC admissions for adolescents do involve legal referrals (De Leon, 2015). The element of legal coercion is viewed as providing an additional incentive for the individual to remain in the TC until she or he has started to internalize the recovery philosophy and lifestyle (Satel & Farabee, 2005). Unfortunately, both self-referred and legally mandated clients often fail to successfully complete the treatment program, and such programs suffer from significant dropout rates (Satel & Farabee, 2005; Work Group on Substance Use Disorders, 2007). However, research evidence points toward the effectiveness of TCs (De Leon, 2015; Vanderplasschen et al., 2013).

Therapeutic communities are not without their detractors. Over the years, lawsuits have been brought against various TCs, alleging physical or emotional harm to the residents. Therapeutic communities are also viewed with suspicion by many who were trained in the more traditional substance rehabilitation model. Retention is a problem for therapeutic communities, just as it is for every other form of substance rehabilitation. In spite of these facts, a meta-analysis of TCs points to the success of these programs, especially when participants remain in treatment and participate in supportive aftercare (Vanderplasschen et al., 2013).

As noted above with outpatient and inpatient treatment programs, TCs are not the answer for all individuals. The very nature of the controlled environment and length of TCs may actually contribute to the challenges of change (Lee, 2016). Despite the positive outcomes found in the research, it is once again important to note that those who are referred to TCs with those who are referred to hospital-based inpatient treatment programs or outpatient treatment programs

may be quite different groups of individuals. Those who complete any of these types of programs may also be quite different from those who enter and leave without completing. Thus, the TC movement is not a panacea for the treatment of SUDs, and further research is needed on all types of treatments and participants, from the individual referred who never attends, to the individual who completes through all aftercare recommendations.

Is There a Legitimate Need for Inpatient Treatment?

Unfortunately, the debate over whether inpatient or outpatient rehabilitation programs are most effective is often fueled by financial or political considerations, not by scientific research (Weiss & Dreifuss, 2015). Some critics of residential treatment point to the Project MATCH Research Group findings in the mid-1990s, which concluded that inpatient treatment is not automatically superior to less intensive treatment methods. The purpose of Project MATCH was to isolate patient characteristics that might predict a better outcome in an outpatient or an inpatient treatment setting, but it failed to accomplish this goal (Rychtarik et al., 2000). Indeed, research has yet to demonstrate a clear advantage of inpatient treatment over outpatient treatment, or the reverse (Mee-Lee & Gastfriend, 2008).

Although clear advantages over outpatient treatment have not been demonstrated by research studies, it has certainly not been recommended that inpatient treatment programs be abolished. For example, some clients with SUDs might benefit more from residential treatment because of the intensity of their addiction, as well as other complicating factors in their lives or histories (Weiss & Dreifuss, 2015).

The Advantages of Inpatient Treatment

It is a mistake to compare those who enter an outpatient substance rehabilitation program with those who are referred to a residential treatment program. These are two distinct subgroups of people misusing substances. Persons referred to a residential program are assessed as needing a *more comprehensive level of care* than those persons who might be referred to an outpatient treatment. Weiss and colleagues (2008) observed that the combination of detoxification and residential treatment programs offers the additional advantage of taking persons who support their addiction through violent crime off the streets.

Residential treatment programs also offer the advantage of allowing intensive focus on environmental issues that contributed to the maintenance of the substance use disorder.

The client might be taught “refusal skills,” or learn alternative behaviors that will help them abstain from further substance use while building a substance-free support system. The inpatient treatment “community” can function as a pseudo-family, guiding the person in acquiring those skills necessary to establish close, non-substance-centered interpersonal supports.

Further, persons referred to residential treatment programs tend to have more medical problems than those persons referred to outpatient treatment. Inpatient programs allow for proper treatment of these medical problems (untreated hypertension or diabetes, for example). Malnutrition is a common problem among those misusing substances, and inpatient residential treatment programs allow medical professionals to address the long-term effects of malnutrition. Further, the level of staff control over the client’s environment helps to discourage continued substance use. A visitor who is a known drug dealer, for example, might not only be refused admission to the treatment facility, but might be informed that the police will be called should he or she attempt to “visit” former customers again.

If a client should attempt to utilize alcohol or drugs while in treatment, staff members in a residential facility are more likely to detect this than are those persons who work in an outpatient treatment program. Staff members are able to establish a routine of individual and group therapy sessions, combined with spiritual counseling, vocational counseling, and ancillary services, to counteract the chaotic lifestyle often seen in those misusing substances. This external structure may be internalized by the person recovering from substance misuse, providing some degree of structure once she or he leaves treatment and begins to live on his or her own. Programs that require participation in community support groups might expose a client to these external support groups for the first time in the person’s life, and serve as a bridge between the residential treatment program and the client’s use of such community supports after discharge.

Disadvantages of Residential Treatment

First, there is mixed evidence about the effectiveness of residential treatment (Weiss & Dreifuss, 2015). Some residential treatment programs become a “revolving door,” admitting and discharging the same client(s) time after time. Also, residential treatment is quite expensive, as noted earlier. It is disruptive to the individual’s established life routine to have to enter residential treatment, and this will interfere with the individual’s ability to go to work and earn a living while the individual is in treatment (Polydorou & Kleber, 2008). Another disadvantage of residential treatment is that patients are usually not stratified as to intensity of need, the result

being that more severely disturbed individuals are often housed with those persons whose requirements are less intense (Larimer & Kilmer, 2000). Residential treatment has often been compared to a concentration camp, but given the clients’ level of dysfunction and substance-induced harm, this comparison is hardly fair. Finally, residential rehabilitation programs may be geographically isolated, preventing appropriate contact between the client and his or her family.

Aftercare Programs

Health care professionals view the SUDs as chronic, relapsing disorders, and the *continuing care* or *aftercare* program was introduced as an aid to abstinence. Such programs have been found to significantly reduce client relapses and increase total days of abstinence (Ritsher, Moos, & Finney, 2000; Smith et al., 2006). The focus of such groups should be on such issues as (a) maintenance of gains made in treatment and (b) helping to prevent a relapse back to active substance misuse. Such groups provide the clients with a safe environment in which to discuss urges to use chemicals again, thoughts triggered by environmental stimuli, and “using” dreams, all of which appear to contribute to relapse, and receive encouragement from other group members in their efforts to abstain.

As part of the last goal, irrational client beliefs (“I can’t cope without a drink!” for example) should be identified and addressed, thus reducing the possibility of a relapse. Clients receiving pharmacological support for their efforts to abstain (discussed in Chapter 33) should be encouraged to take their medications as prescribed as well. A client who reports in group that she or he has not renewed his or her prescription for disulfiram, for example, might be telegraphing an intention to return to active alcohol use, and group members should discuss this with the wayward individual. Client behaviors that might contribute to relapse, such as maintaining a supply of alcohol in one’s home (“but it’s just for friends when they come to visit!”), or frequent a bar (“but everybody knows that the bars have the best pool tables”) or the places where one used to go to obtain chemicals, need to be identified and addressed.

Partial Hospitalization Options

The partial hospitalization option offers several advantages over traditional residential treatment programs, while addressing the costs of inpatient treatment. Such programs allow the client to live at home, but to report to the residential treatment center during the day. The advantage of partial hospitalization is that it allows for a greater intensiveness of treatment than is possible through an outpatient treatment,

while still avoiding the need for expensive residential treatment programs. It also allows the client to start to rebuild strained familial relationships while still having the benefit of the intensive support of the day hospitalization staff. For partial hospitalization programs to be effective, the client should have a stable, supportive home environment. If the client's spouse or other family member should also have an SUD or a serious untreated psychiatric problem, then partial day hospitalization is not an option. If the client's home environment is indeed supportive, then partial day hospitalization may be a viable option in his or her recovery program.

Aftercare Programs

The goal of the aftercare program is to provide support during the client's transition from intensive treatment to self-directed recovery. Such programs are usually conducted on an outpatient basis, and include individual and sometimes group therapy sessions as well as specialized adjunct programs such as a continuation of marital therapy started while the patient was in a more intensive form of treatment, for example.

Aftercare programs are part of the continuum of treatment services (Work Group on Substance Use Disorders, 2007). These programs are often automatically offered to clients following treatment, but research evidence suggests that they should not be mandatory for persons following discharge from treatment. Berg (2003) identified a subgroup of individuals who formerly misused drugs who were (a) stable at the time of follow-up, but who (b) refused to participate in aftercare programs because they did not wish to reawaken memories of their past behavior of actively misusing drugs. For this subgroup of patients, participation in an aftercare program, especially if it includes group therapy, might be counterproductive. Thus, careful screening of each client is necessary before making a referral to an aftercare program to determine which individuals would, and which would not, benefit from an aftercare program.

Halfway Houses

The halfway house concept emerged in the 1950s, providing an intermediate step between inpatient treatment and independent living. If the client should lack a stable support system, a halfway house might bridge the gap between residential and independent living. *Halfway houses* share several characteristics: (1) small population (fewer than 25 residents), (2) short patient stay (less than a few months), (3) emphasis on the use of community support groups, (4) minimal rules, (5) small numbers of professional staff members, and (6) an expectation of total abstinence from alcohol or drugs of misuse. Clients are also expected to work, and they

are assigned tasks within the halfway (cleaning the dishes, housekeeping activities, etc.).

There is mixed evidence about the effectiveness of halfway houses (Reif et al., 2014). This might reflect the different treatment philosophies of the various halfway houses. Some facilities place strong emphasis on continued abstinence, while others make little or no attempt to continue the treatment process. However, since research has repeatedly demonstrated that the longer a person remains involved in treatment activities and community-based support groups the better, this would indirectly support the need for halfway houses (Moos, Moos, & Andrassy, 1999).

Sober Houses

The "*sober house*" is a variant of the halfway house. This is not a form of treatment (Fletcher, 2013) but a transitional step between more intensive forms of treatment and independent living. The sober house should be self-policing, with residents confronting others suspected of either breaking house rules or of using alcohol/drugs. As individuals demonstrate more responsibility and achieve longer recovery periods, they are granted increased privileges until they are ready to assume the task of living on their own without chemicals.

Chapter Summary

There is significant evidence that inpatient or residential treatment is not *always* required to help the person learn how to abstain from further substance misuse. A significant percentage of those persons with an SUD come to terms with that disorder without professional intervention or assistance. Persons who do require assistance often encounter the problem that most therapists or rehabilitation programs only offer one philosophical model to clients, a model that might not meet the client's needs (Mee-Lee & Gastfriend, 2008).

Treatment itself might be carried out on either an inpatient or outpatient basis. Outpatient treatment programs offer an alternative to residential treatment, especially for individuals who have a strong social support system, and for whom there is no coexisting psychiatric or medical illness that might complicate the individual's treatment. An advantage of outpatient treatment programs is that the individual might remain in his home environment, and possibly even continue to work on a full-time basis, depending on when the rehabilitation program activities are carried out. This avoids the need for a reorientation program following residential treatment.

Outpatient treatment programs also offer the advantage of long-term therapeutic support, an option that is not

always possible with a short-term residential rehabilitation program. Such therapeutic supports include individual and group therapies, ancillary services such as vocational counseling, spiritual counseling, urine toxicology testing to detect continued substance use, etc. Outpatient treatment appears to be about as effective as residential treatment programs, but usually for persons who have not misused chemicals for as long those referred to residential facilities. However, outpatient treatment programs do suffer from high dropout rates, and a significant portion of those persons who are initially treated in an outpatient facility eventually require residential treatment.

Residential treatment facilities, in turn, offer advantages and disadvantages over outpatient treatment programs. They

are viewed by many as a drastic step, yet for many persons this is necessary if the individual is ever to regain control over his or her life. The inpatient rehabilitation program offers a depth of support beyond that which might be achieved in an outpatient setting. Such services, including referrals for ancillary treatment as indicated, are often the individual's only realistic hope for recovery from SUDs. While questions have been raised concerning the need for residential treatment, these programs do seem to offer a glimmer of hope for those whose SUD is deeply entrenched. Further, evidence suggests that the length of time that the individual remains involved in treatment or aftercare counseling increases the odds of achieving lasting sobriety, which is the goal of both inpatient and outpatient treatment.

The Treatment of Substance Use Disorders

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 31.1** Identify effective characteristics of a clinician working with substance use disorders
- 31.2** Describe the different treatment modalities that may be implemented to address substance use disorders
- 31.3** Understand the purpose of treatment plans
- 31.4** Consider typical components of continuing care programs

Doctors are men who prescribe medications of which they know little, to treat diseases of which they know less, in human beings of whom they know nothing.

—Voltaire quotes (2015)

Introduction

It is indeed unfortunate that the above quotation from Voltaire¹ is as applicable to the treatment of the substance use disorders (SUDs) today as it was when Voltaire expressed his thoughts about medicine in the 18th century. The substance use disorders have remained the wayward stepchild of the biological sciences in spite of the integration of medicine into the bio/psycho/social model² of the addictions. Some substance rehabilitation professionals have been known to use treatment techniques of which they know little to treat poorly understood substance use disorders in persons who they rarely come to understand are individuals who have suffered often horrendous hardship, abuse, and rejection over the course of their lives.

There are many misperceptions about the process of substance treatment and its effectiveness. For example, the public often views “treatment” as if it were a single entity rather than a generic term for a variety of rehabilitation formats and intensities of therapy (Mee-Lee & Gastfriend, 2015). Further, the public often views treatment as having a fixed duration rather than as a process in which the individual’s progress and needs help determine the duration and focus

¹Voltaire (François-Marie Arouet, 1694–1778). French writer, historian, and philosopher.

²Discussed in Chapter 26.

of the rehabilitation effort (Mee-Lee & Gastfriend, 2015). Finally, many persons seem surprised at the whole concept of an “aftercare” program, believing that once the intensive portion of treatment is finished, the entire rehabilitation program is at an end.

Because of these misperceptions, the question of whether rehabilitation is effective or not has sparked fierce debate in the health care community. Admittedly, treatment for the SUDs is not universally effective. However, the charge has been made that patients with an alcohol use disorder (and by extension the other substance use disorders) receive a lower quality of care than patients with other chronic medical conditions (Bradley & Kivlahan, 2014). When seen in this light, however, arguments that rehabilitation is not effective break down in the face of studies that have found that for every dollar invested in treatment society receives a return of \$13 in reduced health care costs, lower crime rates, and improved productivity (United Nations, 2015).

Unfortunately, by themselves current forms of rehabilitation are unlikely to resolve the problem of drug misuse in the United States (Reuter & Pollack, 2006). Many of the treatment methods that are *least* effective were most deeply entrenched in the rehabilitation system (Miller & Brown, 1997) and may still be, although there has certainly be a greater push for evidence-based treatment methods in more recent decades (Miller & Moyers, 2014). However, there is also much debate about the research findings we have thus far regarding such evidence-based treatments, with some indicating that clinical significance for methods is not the same as significant results within research (Miller & Moyers, 2014). This debate often furthers the inclusion of the least effective methods, with the potential for clinicians to make excuses related to poor methods, pointing in a host of different directions, including blaming the client and the current state of research. This discontinuity between clinical practice and clinical research is an ongoing problem in the addictions treatment field. Many rehabilitation staff members say that they use evidence-based treatments, but then essentially go on to use the same treatment methods that were used when they went through treatment or that they have used in the past (Fletcher, 2013). Indeed, it has been suggested “most alcoholics who become abstinent do so *in spite of* treatment, not because of it” (Tomb, 2008, p. 151). Legal sanctions, another popular social response to the problem of substance use disorders, also do not appear to be the answer³ to this problem: Legal interventions tend to result in high levels of recidivism for both criminal activity and substance misuse. In this chapter, the benefits, advantages, and disadvantages of different forms of substance treatment will be discussed.

³Discussed in Chapter 38.

Characteristics of the Substance Rehabilitation Professional

It is through the therapeutic relationship that healing takes place. Thus, the therapeutic relationship is of critical importance to the healing process and to effectively working with clients with substance use disorders (SUDs). It has been suggested that the rehabilitation professional should have certain characteristics. For example, individuals who are dealing with their own substance use or serious psychological issues of their own should be discouraged from actively working with clients in treatment, at least until they have resolved their own problems. This makes sense: If the counselor is preoccupied with personal problems, he or she will be unable to help the client advance in terms of his or her own personal growth.

The clinician who works with individuals with SUDs must “possess many characteristics, some of which include genuineness, empathy, modeling of the desired behaviors, and an appropriately humorous outlook” (Shea, 2006, p. 13). Further, the professional should be adept at *guiding* clients toward recovery rather than telling them what to do. Most people have the resources to solve their own problems, if they are assisted in finding that solution (Shea, 2006). Thus, the therapist’s job is to assist and guide, not to demand or order the client in his or her search for answers. These skills are especially important during the early stages of treatment, when the client’s commitment toward a major life change is still tentative and weak (Simpson, 2004).

It must be understood that clients who enter treatment do so with different levels of motivation and problem severity (Simpson, 2004). In many cases, clients who enter a rehabilitation program are admitting that they are unable to change their own lives, although, as was discussed in the last chapter, many individuals who enter treatment do so under external motivation. Clinicians with strong interpersonal skills would be better equipped to help the client change. The client’s acceptance of the professional’s efforts to assess them in making this change is one of the most essential characteristics of a successful therapeutic relationship. These relationships are based on mutual trust and openness, as well as the client’s ability to accept external help. Miller (2003) identified several factors that seem to facilitate or inhibit recovery from substance use disorders, as reviewed in Table 31-1.

It will be noted that those factors that facilitate change are very similar to those in patient-centered care. Shared decision making is a central component of patient-centered care, as are providing information about the nature of the disease and the benefits and risks of each treatment option, supporting patients as they work through the decision-making process, and providing support for patients’ decisions (Bradley & Kivlahan, 2014). If the individual’s decision-making abilities

TABLE 31-1 Factors That Facilitate or Inhibit Recovery from SUDs

Factors That Facilitate Change	Factors That Inhibit Change
Empowerment	Disempowerment
Active interest in client as a person	Hostility, disinterest
Empathy	Confrontation
Making client feel need for change	Making client feel that s/he is not responsible for change
Advice on how to change	Ordering client to change
Involving client in the change process	Giving client a passive role
Environment supportive of recovery	Environment does not support recovery

are compromised, the family and caregivers might be made part of the decision-making process (Bradley & Kivlahan, 2014). Unfortunately, the treatment model often used in the United States involves the staff *telling* the patient what the rehabilitation goals and methodology will be without patient input.

Confrontation and Other Techniques

In the latter half of the 20th century, clinical theory, supported by anecdotal evidence, made clinicians believe that heavy confrontation was necessary for the rehabilitation process to begin (Miller & White, 2007). This is now seen as a therapeutic myth that is still often enshrined in rehabilitation training programs. There is little evidence that such confrontation helps the client to begin or make behavioral change (Miller & Rollnick, 2012; Miller & White, 2007). Instead, as the level of confrontation increases, so does the level of client resistance. This makes sense, since one factor that predicts successful treatment is the client's satisfaction with the rehabilitation process (Hser, Evans, Huang, & Anglin, 2004). However, there is also a danger that the health care professional will become too passive, failing to focus on the problems that the client has (or possibly will) encounter(ed) if he or she continues to misuse chemicals (Washton & Zweben, 2006).

In contrast to confrontation, *empathy* for the client's struggle has been found to be more appropriate (Miller & Rollnick, 2012). Where confrontation is necessary, it should be infused with caring and concern for the client, with a focus on their current or anticipated problems (Ramsay & Newman, 2000). The client should not be shamed into conformity, but should be allowed to develop the skills necessary to abstain from substance misuse by utilizing the resources at

hand. This is a slow process, to be sure, but it also empowers the client to then learn that she or he has the resources necessary to change, and how to apply these resources. The professional serves as a guide and confidant, helping the client explore behavioral alternatives while achieving a sense of self-efficacy. Such a therapeutic style places emphasis on the client's ability to change and responsibility for personal change, not heavy confrontation. In this manner, it is hoped that the clinician can guide the client to a substance-free lifestyle.

The Minnesota Model of Substance Use Treatment

Vaillant (2000) identified four factors that were common to all substance rehabilitation programs: (1) compulsory supervision, (2) introduction and use of competing behavior to replace the SUD, (3) new love relationships (in the sense of a commitment to recovery rather than substance use), and (4) increased spirituality and religiosity. The "Minnesota model" of substance treatment met all four of these criteria, and dominated the therapeutic scene for the last half of the 20th century. It still remains a strong influence on both inpatient and outpatient rehabilitation programs (Foote, 2006; Ringwald, 2002).

The Minnesota model was developed in the 1940s and 1950s across three different settings in Minnesota (Spicer, 1993). Dr. Daniel Anderson and Dr. Jean Rossi's involvement at the Willmar State Hospital in Willmar, Minnesota, seems to be the official starting point (Anderson, McGovern, & Dupont, 1999), and it then spread to the small, newly starting Hazelden Foundation, as well as the Pioneer House (Spicer, 1993). The growing influence of Alcoholics Anonymous was viewed by those at these three sites as a means of understanding and working with the alcohol-dependent person (Spicer, 1993).

The multidisciplinary approach to working with those with alcoholism had its start at the Willmar State Hospital (Spicer, 1993). Each person represented a different profession, and thus contributed a different perspective on the client's needs, strengths, areas of weakness, and the issues that needed to be addressed in order to prepare the individual for a life without alcohol. A spiritual advisor by the name of Rev. John Keller was also assigned to the treatment team (Larson, 1982). With his arrival, the staff had "knowledge of medicine, psychology, A.A. and theology together under one roof to develop a new and innovative treatment program" (Larson, 1982, p. 35).

This new treatment model, the Minnesota model, was developed for work with alcohol-dependent persons. It has since been applied to the treatment of all forms of substance misuse. The Minnesota model is centered around the

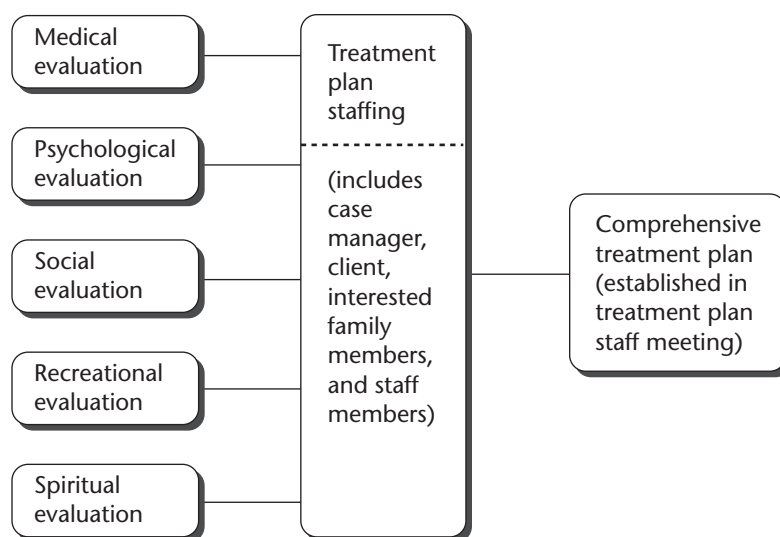


FIGURE 31-1 Flowchart of the Evolution of a Treatment Plan.

treatment team approach, in which the skills of a substance rehabilitation counselor, psychologist, physicians, nurses, recreational therapists, and clergy are brought together to work with the client. Each professional is allowed to make recommendations for the areas to focus on, and the document that emerges from this process is identified as the *treatment plan*. Other interested parties such as family members, probation and parole officers, and the client are also invited to participate in the process of building a treatment plan.

The treatment plan that emerges is, in theory, multimodal, offering a wide variety of individualized goals and treatment recommendations. It identifies specific problem areas that need to be addressed, and behavioral measurements by which each goal could be assessed. A target date for completion of each goal is also identified. The treatment plan itself will be discussed in more detail later in this chapter, but a flow chart of the treatment plan process might look like Figure 31-1.

One strength of the Minnesota model of rehabilitation is its redundancy, and the multi-professional treatment team. The chemical dependency counselor did not need to be a “jack of all trades, master of none,” but could make referrals to other members of the treatment team in response to the client’s shifting needs. This feature helped to make the Minnesota model one of the primary treatment program models for more than 50 years, though under changing health care practices, it has been modified or replaced by other treatment formats in some settings.

Reaction to the Minnesota Model

The Minnesota model has not met with universal approval or acceptance. One early challenge was based on the fact

that, although it was designed for working with alcohol-dependent persons, it was rapidly applied for use with individuals with addictions to other compounds as well, without research into whether the Minnesota model was equally effective with these other forms of drug addiction. However, it is still utilized in the treatment of other SUDs, even as the research evidence seems to trail behind (as indicated by findings by McPherson, Yudko, Afsarifar, & Freitas, 2009, that the model has not yet been shown to be effective in the treatment of CNS stimulant addiction).

The Minnesota model draws heavily on the principles of Alcoholics Anonymous (AA),⁴ and participation in AA is required as part of the program. Yet AA is not in itself a form of treatment, and there is only limited evidence that AA is effective for individuals who were coerced into treatment (Kownacki & Shadish, 1999). Surprisingly, even in cases where there is a wide discrepancy between the spiritual orientation of the rehabilitation program and the individual’s own spiritual beliefs, there was no negative influence on the client’s self-reported desire to drink (Sterling et al., 2006). Such discrepancies did not appear to increase premature termination from treatment, nor did they appear to slow progress in the rehabilitation process, according to the authors. Thus, the apparent contradiction in the Minnesota model in that participants are required to participate in an organization centered on spiritual growth does not appear to be a major issue at this time.

Another challenge to the Minnesota model was the arbitrary decision that treatment should last 28 days. There was little evidence to support a 28-day treatment program,

⁴Discussed in Chapter 35.

although it did become something of an industry standard for a number of years and served as a guide for insurance company reimbursement policies. A grim unintended effect of this process is that many individuals are admitted to a 28-day treatment program based not on his or her needs, but because the insurance companies would only pay for a treatment stay of 28 days! Whereas research suggests that those individuals who remain in treatment for 90 or more days have a greater chance of abstaining from alcohol or drugs, it is not uncommon to read in a treatment program discharge summary that the individual was discharged from treatment after 7, 14, or perhaps 28 days because their insurance benefits had expired.

The Minnesota model was advanced at a time when there was little formal treatment for alcoholism, a factor that resulted in its widespread acceptance (Willenbring, 2010). In spite of the enthusiasm with which it was received and with which supporters defend this program paradigm, further research is needed to suggest that the “Minnesota” model is effective (Hester & Squires, 2004; McCrady, 2001).

Other Treatment Formats for Substance Use Disorders

In the years since the Minnesota model was introduced, and especially since the managed care initiatives of the 1990s, health care professionals have explored a number of alternative treatment formats in working with individuals with SUDs that do not involve inpatient rehabilitation. In this section, we will briefly examine some of the more common treatment models that have emerged.

Acupuncture

This is a form of “alternative medicine” that has on occasion been utilized in the treatment of SUDs. Anecdotal reports suggest that acupuncture has a calming effect on the client and reduces craving for alcohol or drugs. The theory behind this technique is beyond the scope of this text, but in practice small, sterile needles are inserted into specific spots on the body in an attempt to liberate or block the body’s energy. There was limited evidence supporting the effectiveness of acupuncture in the rehabilitation of those misusing substances, which appeared to be about as effective as placebos (Ernst, 2002; Hester & Squires, 2004). This conclusion appeared to be supported by the findings of Margolin and colleagues (2002), who found that acupuncture alone does not appear to be an effective treatment for cocaine addiction. However, more recent research seems to support

the efficacy of acupuncture as a treatment for SUDs in some cases (Baker & Chang, 2016; Chang & Sommers, 2014). Further research is needed to determine whether this form of treatment will be helpful with different types of SUDs, as well as whether acupuncture alone or along with other treatment methods is more effective.

Computer Simulations

With the growing computational ability of computers, it is now possible to utilize “virtual reality” simulations during both acute and extended treatment for substance use disorders. Such computer simulations might either be projected onto the computer screen, or onto the screen of a special visor that the participant wears. The advantage of the latter approach is that the visor provides a wider field of view, thus simulating normal vision. Both methods of computer simulation are especially attractive to younger persons who grew up with computers and computer simulation games.

One advantage of the virtual reality approach is that individualized scenarios can be set up to enable the client to practice situation-specific skills. For example, a program could be set up in which the client and his or her spouse argue, all seen from the client’s perspective. Then the background might change to show what it would look like if the client were walking down the street and entering a favorite bar after the argument. Upon entering the bar, the bartender (a computer simulation) could be programmed to greet the participant by name and ask what he or she would like to drink while other patrons (also computer simulations) also greet the participant by name and invite him or her to join them. The client then could practice refusal skills in a setting in which he or she once consumed alcohol following a marital dispute. After this skill is practiced, then the goal might be for the client to stop before entering the bar following the argument with their spouse, and substitute other behaviors (also included in the simulation) such as calling a friend to meet and talk over a cup of coffee about the argument and how the client might deal with the problem, or going to a local 12-step support group meeting. Technology also allows for virtual 12-step group meetings in which computer-simulated “persons” (specifically built to resemble the actual person) will walk into the meeting room and interact with other participants in real-time meetings. Such virtual reality 12-step groups have the advantage of being available to persons who are geographically isolated, or who need group feedback on a real-time basis, using equipment now used by participants of virtual reality war game simulations, for example.

The application of virtual reality approaches to substance rehabilitation has only just begun, and it is certain

that in the years and decades to come, technology-assisted treatment approaches will become ever more important to the individual's rehabilitation program.

Detoxification

Technically, the term **detoxification** refers to the process of removing any toxin from the body. A second, related definition refers to the medical management of a person's withdrawal from alcohol or drugs (Haack, 1998). One common misperception is that the process of detoxification is a form of "treatment" in itself (Fletcher, 2013). Research has consistently demonstrated that the majority of those individuals who go through a detox program for their SUD will relapse without formal treatment (Craig, 2004). It is for this reason that detox is viewed as a prelude to the rehabilitation process (Fletcher, 2013; Gerada, 2005; Leshner, 2001a, 2001b; McPherson et al., 2009).

The goal of the detoxification process is to offer the individual a safe, humane withdrawal from alcohol or illicit drugs. The patient's safety is assured, to the degree that this is possible, by having a physician who is both trained and experienced in the process supervise the detoxification process. Under the physician's supervision, the detoxification process will be carried out either on an outpatient basis if possible, or on an inpatient basis if necessary. Traditionally, detox from alcohol has been carried out in a hospital, although this is necessary in only 10–15% of alcohol-dependent persons (Anton, 2005; Blondell, 2005). The final decision as to whether to attempt inpatient or outpatient detoxification from alcohol rests upon the attending physician. However, if the individual has experienced only mild to moderate withdrawal symptoms, has no major coexisting medical or psychiatric problems, has a responsible support person who can closely monitor their progress, has not failed at home detox in the past, and has a stable home environment supportive of recovery, it is possible that the withdrawal cycle for alcohol dependence might be carried out at home⁵ (Fletcher, 2013). Persons who are geographically isolated, have experienced serious withdrawal symptoms in past detoxification efforts, or who lack a stable home environment should be referred to a residential detoxification program (Anton, 2005).

The decision to attempt alcohol withdrawal on an outpatient basis is made only after a careful medical examination. Each day, a nurse will stop by the patient's home once or twice a day to monitor the patient's blood pressure, check to ensure that they have abstained from further alcohol use, and monitor the patient's health status as necessary. If the patient

should relapse or show signs of major medical or psychiatric complications, a referral to an inpatient detoxification center or hospital would be necessary (Anton, 2005). *Ambulatory detoxification* from prescribed or illicit compounds is based on the individual's past drug use history and medical status. Some of the drugs of misuse, such as the barbiturates or benzodiazepines, can cause severe, life-threatening problems during detoxification. In some cases, the patient can be monitored at home by another responsible adult and placed on a gradual "**taper**"⁶ regimen to allow them to safely reduce and eventually stop their misuse of these compounds.

If the individual's environment does not permit ambulatory detoxification, or if the person should experience serious medical or psychiatric complications during the detoxification process, a referral to an inpatient detox program is automatically made. Nonprescribed substance use, often justified on the grounds that the person needed some additional assistance during the detox cycle, suggests that urine toxicology testing should be carried out to ensure both that the patient is taking recommended medications and that he or she is in compliance with the regimen (Blondell, 2005). In spite of strident cries from individuals who are opiate-dependent, withdrawal from these compounds is rarely life-threatening,⁷ but because of the tendency for such patients to relapse inpatient detox is usually more successful than outpatient detoxification for this class of medications.

Many rehabilitation professionals believe that detox programs serve a gateway function, guiding the patient into a rehabilitation program. Unfortunately, some treatment centers add a detox component to their rehabilitation program even if the person should not require it, while other programs will refer the individual to only one rehabilitation program exclusively (Fletcher, 2013). This is often justified because many patients fail to go on to enter a rehabilitation program after completing the detoxification process (Miller & Rollnick, 2012). The individual and their family should be provided with a list of available programs in the area, and the decision as to which rehabilitation program the person should enter is made by the person and their family rather than forced upon them as the only option beyond detox. The fact that the patient and family were provided with a list of possible rehabilitation programs that the individual might enter should be carefully noted in the chart to avoid possible conflict-of-interest charges at a later date.

Detoxification programs are subject to a number of abuses. Some individuals will "check into detox" to find a place to hide from drug debts or the media, or to escape from the police. Those struggling with an opioid-use disorder have

⁵A process that has also been called "ambulatory detoxification" or "social detoxification" (Blondell, 2005).

⁶See Glossary.

⁷This is based on the belief that the patient is abusing *only* opioids.

been known to enter a detox program to be cleansed of illicit drugs and allow their tolerance to opioids to drop, making it less expensive for them to return to opioid use upon discharge.⁸ Thus, while detoxification programs provide a valuable service, they are also vulnerable to abuses.

Family/Marital Therapies

Although viewed with a measure of disdain in the middle of the 20th century, family and marital therapies have been shown to be valuable components of substance rehabilitation programs and are now considered an integral part of treatment (Fals-Stewart, Lam, & Kelley, 2009). One goal of such ancillary therapy is to help the spouse and family members learn how to support the patient's efforts to achieve and maintain abstinence (Work Group on Substance Use Disorders, 2007). Another goal is to identify marital conflict issues that might have contributed to the individual's SUD, so that they might be addressed (Fals-Stewart et al., 2009).

The terms **marital and family therapy** are generic terms applied to a number of different therapeutic approaches including the psychodynamic, family systems, structural, and behavioral family therapy approaches. Within the field of substance rehabilitation, the best-known and most common form of family therapy is the **family disease model**, which postulates that substance misuse in the family unit is an illness of the entire family and not just of the person misusing substances (Fals-Stewart, O'Farrell, & Birchler, 2003, 2004). Proponents of this model believe that every member of the family plays a role, and the therapist works to identify the role that the SUD plays within the family. For example, some individuals will use alcohol as a way of punishing their partners, while others will use alcohol to make themselves numb to what they perceive as rejection by their partners.

In families in which a member has an SUD, communication patterns may be confused or unhealthy, supporting the individual's SUD (Alter, 2001). Boundaries within the family may be fluid, or may not exist at all. Familial defenses often become interlocking, allowing the family to maintain a form of stability even in the face of rehabilitation efforts. Power roles within the family with a member with an SUD are often assumed by other family members, who then resist efforts to get them to relinquish these roles so that the now-recovering family member might assume them again. All of these forces contribute to efforts to undermine or resist any effort to change by the addicted individual, including efforts at abstinence.

Given the impact that an individual's SUD has on the marriage and familial unit, marital or family therapy can be a valuable adjunct to treatment, and its importance has repeatedly been demonstrated in the clinical literature (Fals-Stewart et al., 2004). For example, the team of Neto, Labaz, Agular, and Chick (2008) found that social support provided by an adult who is close to the recovering alcoholic (usually the spouse) resulted in significantly longer periods of abstinence in the first 180 days following treatment, with the mean time for relapse being approximately 150 days. Additional research findings suggest that family members participating in a family program increases the completion rate of individuals in treatment (McPherson, Boyne, & Willis, 2016). But family and marital counseling is a specialized area of expertise, which requires extensive training and supervision to be effective. It should not be attempted unless the therapist has the appropriate training and experience in family or marital therapy. Unfortunately, many treatment centers offer what they classify as family or marital therapy that fails to be the intense, dynamic process of therapies in which the marital partners or family members meet with an appropriately trained therapist on a frequent basis (Fletcher, 2013).

Individual Therapy Approaches⁹

One of the inconvenient truths on which addictions counseling rests is that research to date has not been able to isolate the mechanisms through which behavior change takes place (Morgenstern, Naqvi, Debellis, & Breiter, 2013). As a result of this failure to identify these change mechanisms, literally hundreds of theoretical counseling schools of thought have emerged, of which perhaps 10–20 have gained widespread acceptance (Murdock, Duan, & Nilsson, 2012). These theoretical systems include motivational interviewing, the cognitive-behavioral therapies, Gestalt, and psychodrama. These therapeutic paradigms are utilized in the treatment of general mental health problems as well as in substance rehabilitation programs.

Individual therapy sessions offer the advantage of allowing the client to discuss issues too personal to discuss in a group format (victimization issues, sexual orientation, guilt over past behavior, etc.) with an individual therapist with whom the client has an established therapeutic relationship. Depending on the client's assessed level of care needs, individual counseling might be the most appropriate form of treatment for a given individual. Unfortunately, in some treatment centers the person conducting the session might

⁸Unfortunately, it is not uncommon in this situation for the patient to misjudge her or his drug dosage following detoxification, and overdose on opioids because of this (possibly with fatal results).

⁹Substance rehabilitation professionals are most strongly encouraged to *not* use therapeutic techniques for which they have not received the appropriate training and supervised experience.

lack even a high school diploma because the treatment center mistakenly believes that having achieved sobriety is more important than formal education (Fletcher, 2013). Individual therapy should only be carried out by properly trained health care or substance rehabilitation professionals who are well versed in the methodologies, advantages, and risks associated with the treatment format.

Many of the questions raised by Nasrallah (2010b) about individual psychotherapy apply to the substance rehabilitation program that claims to use an individual counseling or therapy component: (a) What is the optimal schedule for psychotherapy? (b) What is the primary indication for individual psychotherapy? (c) Are there conditions for which it is contraindicated? (d) Is there a “loading dose” for individual psychotherapy sessions, after which the individual is most likely to benefit from additional treatment? (e) How long does a psychotherapy session need to be for maximum effectiveness? and (f) Is there a best time of the day in which to conduct psychotherapy sessions? Ideally, most rehabilitation and aftercare programs (discussed later in this chapter) utilize a mix of individual and group therapy formats. However, some programs do not provide the frequency of individual therapy sessions that would be appropriate for the individual (Fletcher, 2013).

COGNITIVE-BEHAVIORAL THERAPIES

The term *cognitive-behavioral therapy* has evolved over the past two decades to include cognitive therapy, cognitive-behavioral therapy, contingency management, self-monitoring, problem-solving, assertiveness training, behavioral rehearsal, and the social learning therapies (Macgowan & Engle, 2010). The cognitive-behavioral therapist will often draw from a wide range of different therapeutic schools of thought, making the exact definition of a behavioral treatment approach very difficult (Macgowan & Engle, 2010). Traditionally, cognitive-behavioral approaches to rehabilitation of those misusing substances involve 10–20 individual therapy sessions. Cognitive-behavioral approaches to substance use disorder appear to be moderately effective for both adult and adolescent clients, although the clinical literature supporting the latter is more limited than is the pool of literature supporting the use of cognitive-behavioral therapies with adults who misuse substances (Macgowan & Engle, 2010; Winerman, 2013).

Cognitive-behavioral therapies help the individual learn inhibitory control techniques, in part by confronting irrational thoughts or beliefs that the client might have. One such irrational thought might be “I *cannot* endure the urge to use!” The therapist might help the individual look back to when they experienced similar episodes of drug-use urges where they did not resort to drug use, examine how they were able to endure that period without engaging in the use of chemicals, explore whether similar coping strategies might work

under the present circumstances, and point out to the individual how their past behavior proves that they can endure the urge to use chemicals without giving in to it.

MOTIVATIONAL INTERVIEWING

The theoretical roots of the motivational interviewing (MI) approach to working with a person misusing substances can be traced back to the social learning and cognitive-behavioral therapies (Macgowan & Engle, 2010). Over the years, the exact definition of motivational interviewing has become blurred as different therapeutic techniques have fallen under the umbrella of MI. **Motivational interviewing** is a therapeutic technique used in short-term interventional therapy that places great emphasis on helping individuals identify how they are currently living and how they wish to be living in the future. This process involves a collaborative effort between the therapist and the client to identify (a) problem behaviors and (b) the client’s view of effective behavior change (Macgowan & Engle, 2010). In motivational interviewing sessions, the individual is not required to admit having a substance use disorder, but only to consider the possibility that a lifestyle change is in his or her best interest. Open-ended questions, affirmation for signs of progress,¹⁰ reflection of the client’s comments, and summarization of progress made to date are all part of the therapeutic approach used by the therapist who draws on MI techniques (Miller & Rollnick, 2012; Winerman, 2013).

The pool of clinical literature supporting the effectiveness of MI is mixed, with some researchers failing to find a significant difference in outcome between clients who were treated by a therapist who used MI and control groups. MI appears to hold promise as a brief interventional technique for clients who are seen for a short-term (one to five sessions) therapeutic interventions (Macgowan & Engle, 2010).

CONTINGENCY MANAGEMENT

The **contingency management** approach uses immediate rewards with tangible incentives for abstinence (Winerman, 2013). A person whose urine toxicology tests were clean for signs of illicit drug use might receive a point for each sober day, which can be applied against the purchase of a desired item such as a personal radio that is available for 30 points. Sometimes local businesses will contribute items that the client can work toward or offer employment opportunities in return for proven abstinence, and cash incentives such as a pay increase are always welcome (Winerman, 2013). Paradoxically, although the value of the reward item would appear to be modest at best in comparison to the immediate rewards

¹⁰Miller and Rollnick (2012) advocated the technique of affirming the client for every sign of forward progress. If the individual reports that they drank to the point of intoxication only five nights out of seven in the past week, as opposed to six out of seven nights in the week before that, they would receive positive feedback from the therapist for this sign of progress.

of the drugs of misuse, many individuals place great emphasis on earning a desired reward item. When used appropriately, contingency management programs provide a powerful tool in the fight against the SUDs.

PSYCHOANALYSIS

This therapeutic school of thought has a long history of being tried with those misusing substances, with at best limited success. A central tenet of the psychoanalytic theories is that the individual's emotional growth is blocked by unresolved emotional conflicts. In the face of such unresolved issues, individuals are postulated to use characteristic behaviors and defenses to protect themselves from the immediate experience of anxiety brought on by these unresolved issues, albeit at the expense of long-term adjustment. Many misusers of marijuana, for example, speak of the brief periods of euphoria that they experience while using marijuana as a way to escape from their problems. Another example is Khantzian's (2003b) theory that individuals with anxiety disorders might be drawn to the use of compounds such as alcohol, the benzodiazepines, narcotics, marijuana, and the increasingly rare barbiturates because of their **anxiolytic**¹¹ effects.

The effectiveness of psychoanalysis in treating persons with a substance use disorder has been debated. In theory, the therapeutic relationship provides the framework in which neural reorganization takes place, counteracting the neural network changes induced by the drugs of misuse (Feldstein-Ewing & Chung, 2013). Many therapists from different schools of therapy will borrow selected psychoanalytic techniques to assist them in their work with individual clients; however, doing this borrowing is not considered *psychoanalysis*. The therapist is just borrowing certain techniques to help with his or her work. True psychoanalysis is labor-intensive, the costs are often prohibitive, and the technique does not lend itself to treating large numbers of those misusing substance. However, contrary to popular opinion, psychoanalysis is receptive to change as new information about the central nervous system is uncovered. The therapeutic learning process initiated by psychoanalysis can be a valuable adjunct to treatment, and as scientists learn more about how psychoanalysis initiates neural-cognitive reorganization, it might become an even more effective tool for the addictions counselor.

Group Therapy Approaches¹²

Group therapy is the most common modality through which psychosocial change is attempted for those struggling with

addictions (Brook, 2015). Unfortunately, the term **group therapy** is a generic term for a wide variety of therapeutic approaches carried out in a group setting, including cognitive-behavioral therapy, rational-emotive therapy, Gestalt therapy, psychodynamic group therapy, psychodrama, assertiveness training, etc. (Work Group on Substance Use Disorders, 2007). There is little evidence that the type of group counseling used in most treatment centers, a form of 12-step–based discussion, is effective (Tomb, 2008).

It is thought that the individual re-creates his or her family of origin within the group setting, affirming the tenet of the various forms of group therapy that it is an interactional process (Yalom & Leszcz, 2014). By re-creating their family of origin within the group, individuals have the opportunity to relive the relationships that caused them so much trauma and to resolve issues from their family of origin (Brook, 2015; Yalom & Leszcz, 2014). To achieve this goal, the group leader should have received extensive training in the theory and applications of group therapy, something that is often lacking in many treatment centers, where the group leader might lack even a high school diploma (Fletcher, 2013). There is debate as to whether it is appropriate to intermix persons at different stages of the recovery process in the same group, or if the rehabilitation center should offer different groups for persons at different stages of recovery (Fletcher, 2013). In the therapy group setting, those misusing substances might learn how to form healthy, non-substance-centered relationships while enhancing self-esteem (Brook, 2015).

Cognitive-behavioral therapies can be used in a group therapy format if the group leader has received the proper training to call upon this treatment modality. Group members learn to help each other identify self-defeating thoughts, the painful emotions that are caused by these thoughts, and ways to replace these unhealthy thoughts with more appropriate thoughts. Personality-disordered individuals, for example, often utilize a black-and-white interpretation of the world around them (“*Everybody is against me,*” or “*I can’t do anything right,*” for example), a cognitive pattern that enhances their frustration and tendency to misuse chemicals. A psychodynamic therapy group could allow a client to better understand the psychological forces that supported his or her addiction, while a psychodrama group format might allow the client to resolve conflicts that have blocked recovery efforts to date through appropriate simulations.

One very useful form of treatment group is the *coping skills group*. Many of those individuals with substance use problems began to misuse chemicals when they were children or adolescents, blocking the process of developing strong interpersonal coping skills (Monti, Kadden, Rohsenow, Cooney, & Abrams, 2002). Social skills training might

¹¹See Glossary.

¹²Substance rehabilitation students who are in training are encouraged to explore the various forms of group therapy through appropriate training under the supervision of a properly trained professional.

include substance use refusal skills training as well as helping the patient learn how to engage in non-substance-related pleasant activities (Marinchak & Morgan, 2013). Refusal skills training might take place within a group setting, where different group members take on different roles to help the individual learn how to refuse opportunities to use chemicals. Social skills training programs might help a client learn interpersonal skills to engage in non-substance-centered recreational activities, as well as to learn how to feel more confident when interacting with others.

While group therapy formats are very useful in the rehabilitation of those misusing substances, it is necessary to carefully screen potential group members. Acutely suicidal or homicidal clients should be referred to individual therapists or hospitalized immediately for psychiatric treatment, depending on the individual's needs (Brook, 2015). Persons who are unwilling or incapable of maintaining group confidentiality should not be admitted or retained in the group (Brook, 2015). Some persons feel threatened in the group environment and might do better with intensive individual psychotherapy (Fletcher, 2013). Individuals who are in the acute stage of a psychotic episode should be excluded from substance therapy groups, as should group members who wish to utilize the group setting as a venue for selling drugs (Brook, 2015). These rules apply to community-based self-help groups as well as institutionally based therapy groups. However, when these rules are observed, therapy groups might play a major role in the individual's rehabilitation from a substance use disorder.

Biofeedback Training

A number of studies have been carried out investigating the applicability of biofeedback programs to substance rehabilitation. **Biofeedback** is a process in which the individual is provided real-time information about internal body functions such as brain wave or skin resistance patterns. With proper training and feedback from the appropriate device, the individual learns to modify body functions such as muscle tension, skin tension, brain wave patterns, heart rate, etc., without the use of alcohol or drugs. This discovery in itself often helps a client understand that it is possible to change body states, such as relaxing, without the use of chemicals. As a result of this process, biofeedback programs encourage the development of self-efficacy as the patient develops skills in changing body states once thought to be alterable only through the use of chemicals. There is preliminary evidence that supports the use of such techniques in rehabilitation programs (e.g., Eddie, Vaschillo, Vaschillo, & Lehrer, 2015), although further research is needed.

Clinical research has suggested that persons with substance use disorders demonstrate different brain wave patterns,

which possibly reflects a neurological predisposition to the development of SUDs. Neurofeedback, or brain wave biofeedback, is "less than mainstream treatment" (Trudeau, Sokhadze, & Cannon, 2009, p. 241) for the substance use disorders. However, it does appear to be a promising adjunctive treatment modality for the process of rehabilitation. Follow-up research conducted 3 years after participation in a substance use rehabilitation program that included neurofeedback found that 85% of the men in the study reported consistent reduction in or abstinence from alcohol (White & Richards, 2009).

Neurotransmission involves electrochemical signals being passed from one neuron to another. These signals can be amplified and recorded. The pattern of neurotransmission signals can then be grouped together by the wave frequency of the signals. "Theta" band patterns of brain activity have been found to accompany the process of "reprogramming" the brain, and are accompanied by subjective experiences such as serenity and relaxation combined with a breakdown in ego defenses¹³ (White & Richards, 2009). By learning to achieve this state of mind without the use of alcohol or drugs, it is theorized that the individual's motivation for substance use will be reduced or eliminated and the individual's sense of ego mastery improved. While this adjunctive treatment approach appears to offer promise in the rehabilitation of select individuals who misuse substances, large-scale studies into the applicability of neurofeedback are limited at this time (Trudeau et al., 2009).

Harm Reduction¹⁴ (HR) Model

In contrast to the Minnesota model is the *harm reduction (HR) model*. The HR model does not attempt to help the individual abstain from chemicals, at least not at first. It is based on the assumption that it is possible to change the behavior(s) of individuals who have SUDs over time, reducing the immediate consequences of their continued substance misuse. Eventually, it is hoped, the individuals will accept abstinence as a goal, but even if they do not, they are reducing the damage being done by their use of chemicals. Nicotine replacement therapy is one example of this process. Many individuals find it difficult to stop using the nicotine replacement therapy they used in their smoking cessation program. However, their continued use of nicotine in the alternate form reflects the intake of just one chemical: nicotine. There are over 4,500 known compounds in cigarette smoke, including many known to cause cancer, so continuous nicotine therapy avoids

¹³Effects that sound suspiciously like the reasons offered by those misusing drugs for their drug use.

¹⁴Also known as *harm minimization*.

exposure to at least 4,499 of the other compounds found in cigarette smoke.

Another good example of the HR model is opioid agonist replacement¹⁵ programs using methadone or buprenorphine. It is thought that by providing the opioid-dependent person medication in a controlled manner, the individual will be less likely to share needles, inject illicit drugs, engage in criminal behavior, etc. Non-infected individuals who use intravenous opiates and who are placed on methadone maintenance programs have been found to cut their risk of contracting HIV infection¹⁶ by 54%, which is an additional benefit of the methadone maintenance program concept (MacArthur et al., 2012).

Needle exchange programs are also viewed as a form of harm reduction. Because many infectious diseases can be spread through the sharing of contaminated needles,¹⁷ needle exchange programs help to limit the spread of infections that both destroy the health of the individual using intravenous drugs and ultimately result in increased Medicare and Medicaid costs or higher insurance premiums. If a needle exchange program prevents just one or two new cases of an infection such as HIV per year in a given community, the program will have paid for itself (Reuter, 2009). Unfortunately, in spite of the obvious advantages of this process, there is strong resistance toward needle exchange programs in many regions of this country (Reuter, 2009).

Hypnosis

There has been little systematic research into the effectiveness of hypnosis in treating SUDs. The limited research that has been carried out usually involves the use of hypnosis to treat nicotine addiction, and there is little evidence to suggest that this treatment modality is viable in the long term (Work Group on Substance Use Disorders, 2007).

Videotape/Self-Confrontation

In the late 1980s and early 1990s, videotapes were made of the individual shortly after admission to a detoxification unit. This was viewed as a technique that would show the client what he or she looked like under the influence of chemicals, in the hope that it would provide a degree of motivation for the client to discontinue the use of alcohol or drugs, or at least seek help for his or her SUD. There is little data to support this technique, and some data suggests that

it might actually contribute to higher client dropout rates (Hester & Squires, 2004; Miller & White, 2007). A few programs still utilize this procedure, although for the most part it has been discontinued by treatment and rehabilitation programs.

Yoga or Meditation

As is true with hypnosis, there has been little systematic research into the possible application of yoga or similar relaxation procedures in the treatment of substance use disorders. Initially it appeared that there was a rich body of research data supporting the use of yoga as a means to reduce stress, and it was reported to be a useful adjunct in the treatment of depression (Kozasa et al., 2008). However, Farias and Wikholm (2015) identified a bias in the reporting of study results: “Findings of moderate positive effects were inflated, whereas non-significant and negative findings were unreported” (p. 28). Meditation, the authors asserted, was not for everybody. Some practitioners experience muscle twitches, intrusive thoughts that might center around sex, depressive symptoms, anxiety, or violence, as well as trembling, panic reactions, hallucinations, terror, mania or depression, or outright psychotic reactions. These effects are experienced by both novice and experienced meditators, according to the authors, even if they were experienced in the practice of meditation. Thus, this treatment process, once thought to enhance *mindfulness*¹⁸ and as a possible means to enhance neuroadaptive change in the brain (Witkiewitz, Lustyk, & Bowen, 2013), needs further research. Even when used properly, the effects of meditation often require extended periods of training and practice before maximum effects are achieved (Richard, Lutz, & Davidson, 2014), which is contrary to the expectation of immediate reinforcement seen so often in persons with a substance use disorder. Thus, the various meditation techniques currently in use might not be a panacea for substance rehabilitation, as had originally been thought.

The Treatment Plan

The substance rehabilitation professional will have a wide range of techniques, many of which are briefly discussed above, to consider in working with a client misusing substances. The therapist and client should together develop a *treatment plan* to guide the client during the rehabilitation

¹⁵Discussed in Chapter 33.

¹⁶Discussed in Chapter 36.

¹⁷Discussed in Chapter 34.

¹⁸Perhaps best conceived as a measure of being grounded in one's environment.

process. The treatment plan is based on the information obtained during the assessment process, as discussed in Chapter 28. It “serves as the plan of action for pursuing the identified goals of treatment” (Connors, DiClemente, Velasques, & Donovan, 2013, p. 96). The exact format of the treatment plan varies from one rehabilitation center to another depending on the treatment methods being utilized and the certification requirements for that specific health care facility. However, the treatment plan should be a written document, which in some states is a required part of a rehabilitation program and is viewed as a legal document.

All treatment plans share certain similarities. First, the treatment plan should provide a brief summary of the problem(s) that brought the client into treatment. An example of this might be that the “Client has a severe AUD.” Some treatment plans include a brief summary of the client’s physical and emotional health, sometimes in the client’s own words. The generalized statements of *goals* and specific *objectives*¹⁹ are identified. Using the example cited above, the objective might be “Client will successfully complete alcohol detoxification process as measured by staff assessments of Pt status, within 5 days.”

Next there is a summary of the *discharge criteria*, listing the steps necessary for the client to accomplish in order for treatment to be completed successfully. Using the example cited above, the client’s progress in ingesting an adequate diet, which may counteract some of the dietary deficiencies associated with a severe AUD, could be stated as: “The client will consume 80% of meals provided 95% of the time for 3 days, as measured by staff report.” Finally, there is a summary of those steps that are to be made a part of the client’s aftercare program (discussed later in this chapter). Again, using the hypothetical example above, this might be a statement such as “Client to identify a rehabilitation program that [she or he] wishes to enter by time [she or he] is deemed medically ready for discharge, and arrangement to enter that treatment program.”

Another example of a treatment plan goal for a hypothetical 24-year-old misusing multiple substances (cocaine, alcohol, marijuana, and occasionally benzodiazepines or opioids), who has a 3-year history of misuse of these compounds, might be as follows:

Problem: Client has been addicted to chemicals for the last 3 years, by self-report.

Long-term goal: Total abstinence from alcohol and drugs.

Methodology: (1) Successful completion of detoxification program, as measured by staff and Pt report.

Methodology: (2) Successful completion of residential Tx program

Methodology: (3) That Pt take naltrexone as prescribed 95% of the time.

Methodology: (4) That Pt have “clean” urine test results 100% of the time, for 180 days as measured by laboratory reports.

Methodology: (5) That Pt identify in community five support group(s)²⁰ and join at least one to begin to develop substance-free support system.

Methodology: (6) That Pt identify substance-free housing before discharge, or within 30 days of admission to treatment.

Each of the target goals might be modified, or additional goals added as needed. For example, a patient who indicates that she or he “just can’t say ‘no’ to drug dealers” might have the additional objective added to the treatment plan:

Methodology: (7) That Pt demonstrate appropriate refusal skills in role-play simulations 100% of the time, as measured by staff report and Pt report of comfort level using these techniques.

The treatment plan should be a dynamic document that is modified as additional client needs are identified. For example, if an individual were to lose a close sibling in a motor vehicle accident while in a rehabilitation facility, a new long-term goal of helping the client come to terms with his or her feelings of loss and grief without the use of illicit drugs might be an appropriate addition to the treatment plan. The methodologies might include:

Methodology: (1) That Pt participate in 5–10 grief counseling sessions with pastoral counselor prior to discharge from treatment.

Methodology: (2) That Pt write a memorial letter to lost sibling within 2 weeks and discuss same with individual therapist at end of that time frame.

Methodology: (3) That Pt identify fitting memorial for lost sibling within 30 days and implement same at time of their choosing.

Methodology: (4) That Pt join grief group of own choosing and attend three (3) group meetings prior to discharge.

¹⁹A goal is a generalized statement, such as “I want to lose weight.” An objective is a measurable expression of that goal, such as “I want to lose ten pounds.”

²⁰This does not automatically refer to 12-step program groups since church prayer groups, informal mutual support groups, or any of the alternative groups that have emerged as a reaction against the 12-step program movement.

Methodology: (5) That Pt visit grave of lost sibling with staff person of choice within 30 days to end this phase of relationship with the sibling and start a new form of relationship with lost relative. Pt to discuss feelings about this process with staff member of choice on an individual basis for 1–5 hours at time of own choosing.

In this manner, the treatment plan is modified to accommodate changes in the client's status while in the rehab program, reflecting the dynamic nature of the treatment plan and the rehabilitation program itself.

Aftercare Programs

Because the substance use disorders are viewed as chronic, relapsing disorders, treatment does not end with the individual's discharge from an inpatient or outpatient rehabilitation program. Rather, participation in a *continuing care* or *aftercare program* is recommended. Such programs have been found to significantly contribute to client abstinence rates (Ritsher, Moos, & Finney, 2000; Smith et al., 2006). Aftercare programs work on the assumption that rehabilitation does not end with discharge from intensive treatment, but that this is the first step the client takes on the road to long-term recovery.

These aftercare programs usually are carried out in a group format, and focus on issues such as (1) maintenance of goals made in treatment and (2) helping the individual avoid relapsing back to active substance use (McKay et al., 1998). Individual therapy sessions with a professional rehabilitation counselor are utilized as an adjunct to the group therapy sessions. A major component of aftercare programs is helping the client identify mistaken beliefs that might contribute to relapse ("It's all right for me to drink beer, but I have to stay away from the hard stuff," or "Marijuana can't hurt you, it's natural, and natural things can't hurt you!"). Another goal of an aftercare program is to help the client learn self-monitoring skills to help him or her take responsibility for his or her recovery program. Such self-monitoring skills are a crucial part of an aftercare program because it has been found that "the benefits of abstinence in the first year operate in part through . . . building self-efficacy to abstain from alcohol use" (Maisto, Clifford, Stout, & Davis, 2008, p. 735). An important component in the development of such self-efficacy is the identification of high-risk situations in which the client is more likely to relapse²¹ (being around those who are abusing alcohol or illicit drugs, as suggested in the hypothetical

examples offered earlier in this paragraph) and the development of coping skills through which the client might deal with such high-risk situations.

Many aftercare programs require that participants attend community self-help group meetings on a regular basis.²² Aftercare groups might help clients learn to address medical issues such as chronic pain without relapsing, and offer feedback, guidance, and support for clients addressing such needs as transitional housing, employment, guidance toward appropriate post-treatment family or marital counseling, and encouragement for the client to report to the group any urges or thoughts that might contribute to a relapse. Should the client relapse, the group should offer encouragement as the client struggles to rebuild his or her recovery program, and help her or him examine his or her previous recovery system to identify problem areas that may have contributed to the relapse.

The Treatment/Research Disconnect

Many treatment programs claim to use "evidence-based" treatments. In reality, many clinicians in substance rehabilitation often pay little attention to the research literature, and the treatment format for their rehabilitation centers continues essentially unchanged for years. An untold number of treatment professionals use the "what worked for me will work for you" approach, making little or no effort to review new clinical research, much less integrate it into their practice (Fletcher, 2013; Winerman, 2013). To be fair, treatments that appear promising in the research setting do not necessarily work in the field, but the willingness to review the clinical literature and accept new, research-supported treatment approaches where appropriate is the hallmark of an effective therapist.

Chapter Summary

This chapter reviewed some of the characteristics of the rehabilitation professional, as well as some of the varieties of treatment formats. Individual therapy sessions are often viewed as ancillary to the residential process, although in reality such therapy might be the most appropriate level of care for the client. The need for the therapist to develop a formal treatment plan was discussed, as were various treatment modalities such as detoxification from chemicals, biofeedback, marital and/or family therapies, and group psychotherapy.

²¹Relapse prevention is discussed in Chapter 32.

²²Discussed in Chapter 35.



CHAPTER 32

The Process of Treatment

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 32.1** Understand the process of treatment for SUDs
 - 32.2** Identify the stages of recovery from SUDs
 - 32.3** Consider whether abstinence should be the goal of treatment
 - 32.4** Outline specific points that should be addressed in relation to particular substances when treating SUDs
 - 32.5** Review reactions to the concept of treatment for SUDs
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Introduction

It is common for the average person on the street, and many persons in the health care field, to speak of recovery from a substance use disorder (SUD) as if it were a single step. In reality, the SUDs are often incorrectly viewed as conditions that are acute and treatable using brief treatment. (“Addiction recovery,” 2005, p. 1, italics added). In contrast to this perspective, substance rehabilitation programs should be viewed as a form of *disease management* similar to the disease management programs developed for hypertension or diabetes (McLellan, 2008, 2015). However, even experts in the field of addictions have trouble defining what is and is not part of “treatment” (Fletcher, 2013). Different rehabilitation facilities utilize differing methodologies, although the majority of inpatient or outpatient treatment programs use the Alcoholics Anonymous (AA) 12-step model as a component of the program (Fletcher, 2013).

In the past decades, the concept of rehabilitation programs as a form of disease management for the SUDs has emerged. As is true for the treatment of chronic medical conditions such as heart disease and diabetes, the individual with an SUD may experience periods of relative stability interspersed with acute exacerbations of his or her disorder. Such acute exacerbations of the core illness will require innumerable visits with health care providers, or, in the case of the SUDs, various rehabilitation professionals. This process parallels the process of disease management for other chronic medical conditions. In this chapter, the mechanics of rehabilitation programs will be reviewed.

The Decision to Seek Treatment

The most important factor in recovery from any psychiatric disorder, including the addictions, appears to be *readiness to change* (Mintz, 2011). There is an emerging and exciting body of evidence suggesting that persons who enter rehabilitation program on a voluntary basis begin to alter their substance use behaviors in the days or weeks prior to their entry into treatment (Willenbring, 2010). This would suggest that the actual admission to treatment is the culmination of the decision to end or reduce one's alcohol or drug use, in effect providing a behavioral measure of the individual's commitment to change (Willenbring, 2010).

Clients enter a rehabilitation program for a number of reasons, and vary in their motivation for a major life change such as abstinence from a desired substance (Cooney, Kadden, & Steinberg, 2005). The assessment process should identify the level of substance misuse, as well as the severity of the consequences of that SUD for the individual (liver failure, a lengthy prison sentence, etc.) (Kessler et al., 2001). Persons who enter a formal rehabilitation program tend to be more impaired, and to have more severe life problems, than those who are able to abstain without entering a formal treatment program (Moos, 2003). People who seek professional assistance with an SUD usually have been addicted for 5–8 years, or have engaged in heavy substance misuse for 10–19 years prior to seeking treatment (Kessler et al., 2005). Substances that result in a greater level of immediate impairment (cocaine, for example) will seek treatment earlier than those individuals who are addicted to alcohol, which requires time before its negative effects begin to manifest (Kessler et al., 2005). Further, as Willenbring (2010) suggested, the alcohol use disorders might follow different courses, raising questions about whether the treatment methods designed for persons with one form of alcoholism might be appropriate for those with another. All of these issues must be considered during the treatment planning process.

Methods of Treatment

There are different therapeutic methods utilized in the therapeutic process. Although most treatment centers will claim to use those methods that have been scientifically supported, this is often not the case, and many rehabilitation counselors adapt a “this is what worked for me when I was in treatment so that is the method that I will use” attitude (Fletcher, 2013). In this section, we will examine three evidence-based rehabilitation methodologies.

Motivational Interviewing

The motivational interviewing process is based on several core concepts, including that personality (or behavioral) change is best if motivated from within the individual rather than forced upon that person by outside forces. To this end, **motivational interviewing** (MI) invokes a collaborative approach with the client to assist the individual to make the decision to seek change, with compassion being part of the spirit of providing MI (Miller & Rollnick, 2012). Other core elements of motivational interviewing include expressing empathy for the client, helping the client see that there are discrepancies between his or her goals and values and his or her behavior, realizing the client has autonomy in relation to change, and supporting the client during the change process (Miller & Rollnick, 2012). This change process may often involve distinguishing between *change talk*, which is the client's “statements that favor change,” and *sustain talk*, which is the client's “arguments for not changing” (Miller & Rollnick, 2012, p. 7).

Initial research studies were quite supportive of MI and its application to the treatment of alcohol use disorders, yet some long-term (5-year) follow-up studies have failed to demonstrate increased efficacy of MI approaches to treatment as compared with nondirective therapy approaches, or no counseling at all (Adamson & Sellman, 2008). However, meta-analytic research indicates that MI is beneficial across a broad range of medical settings and medical issues, including alcohol and drug misuse (Lundahl et al., 2013). Research currently points to the active components of MI being the relationship that is developed through the counselor's relational and technical skills to bring about and reinforce change talk (Magill et al., 2014; Miller & Rose, 2009). There is a need for continued research into the elements of MI that are effective, and those which must be modified to enhance efficacy.

Cognitive-Behavioral Therapies

The term **cognitive-behavioral therapy** (CBT) is an umbrella term that includes a number of therapeutic systems with many similar elements. One cornerstone of all cognitive-behavioral therapeutic systems is that the individual has developed a series of false or irrational assumptions on which his or her SUD rests. These core assumptions are expressed through the individual's thoughts, or “self-talk.” These messages that the individual sends to him- or herself then help shape the individual's self-concept and how they view others. An example of one such thought is: “I can't deal with the stress of my job without using [X].” Another irrational thought might be “I have to please my spouse to avoid his or her violent behavior. If I am successful in this endeavor I will be able to feel good about myself.”

Cognitive-behavioral approaches are usually carried out in a series of either group or individual therapy sessions designed to help the individual identify these irrational thoughts and correct them. Written homework assignments are commonly used by the professional to help the client work on their recovery between sessions. Black-and-white messages to the self, such as “everybody is against me,” are identified and the evidence supporting that self-talk is reviewed to determine if this is an accurate summary of the individual’s interpersonal relationships. The individual’s use of “demand words,”¹ which reflect black-and-white thinking, makes the individual vulnerable to failure and potential relapse. The differences between setting a goal (“I would like to . . .”) and the demand (“I have to . . .”), and the relationship of such perfection demands to the individual’s substance use disorder are explored. In this example, the goal of helping the individual start to set goals rather than demands is explored, and the relationship between such demands and feelings of inadequacy and anger that result when the person fails to meet their self-imposed demand, and how such thoughts contribute to substance use are explored. There is a vast amount of research supporting cognitive behavioral therapies across a broad spectrum of presenting issues. Interestingly, recent research has found that combining MI and CBT shows promise, particularly with those with co-occurring AUD and depression (Riper et al., 2014).

Voucher-Based Reinforcement

The process of **voucher-based treatment** involves the distribution of vouchers worth a certain number of “points,” or even credit at a local store, for periods of abstinence confirmed through urine toxicology testing. Such a program might award a voucher the client could use to buy a desired item (stereo, etc.), if he or she could accumulate the desired number of points (in this hypothetical example, perhaps 50 points). Such approaches are combined with more traditional forms of addiction counseling to reinforce the early stages of abstinence, and, if the individual is failing to earn vouchers, to identify the obstacles that prevent the individual from achieving this goal. The relationship of such obstacles to the individual’s substance misuse is explored, and new methods of dealing with the identified problem are devised. Actual money is not used, as this would be a relapse trigger for the client, but points that could only be traded in at a specified

store would lack the potential to serve as a relapse trigger, and this process has been found to enhance abstinence in the early stages of recovery. Support for voucher-based reinforcement has been shown through meta-analytic research (Lussier, Heil, Mongeon, Badger, & Higgins, 2006), although more recent evidence shows its effectiveness is time-limited to the first 6 months (Benishek et al., 2014).

A number of other therapeutic systems have been suggested over the years; however, the efficacy of these programs has not been supported, and so they will not be discussed further in this text. However, experienced addictions counselors will often “borrow” specific techniques from one therapeutic approach or another to establish an individualized treatment program for each person.

The Stages of Recovery

For decades, clinicians have struggled to develop a system that facilitates recovery from the substance use disorders. This process is complicated by the fact that there is virtually no research into the natural history of the SUDs! Indeed, there is a chasm between strongly held clinical beliefs and the research data. The former postulates that the substance use disorders are chronic, progressive conditions, while clinical research suggests that a significant percentage of those persons who meet the diagnostic criteria for an SUD in their late teens or early twenties will either have discontinued or at least greatly reduced their substance use by their late twenties (Heyman, 2009). Those persons who are most likely to continue to have an active SUD as they progress through life are those who have a concurrent psychiatric or medical problem (Heyman, 2009).

To better understand the recovery process, a number of different stage recovery models have been proposed, thus illustrating that recovery from a substance use disorder seems to be a process. The most widely known stage recovery model was introduced by Prochaska and DiClemente in the waning years of the 20th century (Prochaska, 2002; Prochaska, DiClemente, & Norcross, 1992). This model postulated that the individual moved from one stage to the next on his or her road to recovery, and that the needs and characteristics of persons in different stages of change differ (Connors, Donovan, & DiClemente, 2001; Sadock, Sadock, & Ruiz, 2015).

The first stage in this model is that of **precontemplation** (Blume, 2005; Connors et al., 2001; Norcross, Krebs, & Prochaska, 2011; Prochaska, 1998, 2002; Prochaska, Redding, & Evers, 2013). The individual who is in this stage is still actively misusing chemicals, and has no thought of trying to abstain from alcohol or illicit drugs in the next 6 months (Prochaska et al., 2013). If the person has thought about

¹Examples of which include “should,” “have to,” “got to,” “must,” and “ought to,” or their negation such as “should not,” etc. In Alcoholics Anonymous meetings, members are often admonished not “to should all over yourself,” illustrating how members of the group recognize the self-destructive nature of these behavioral demands.

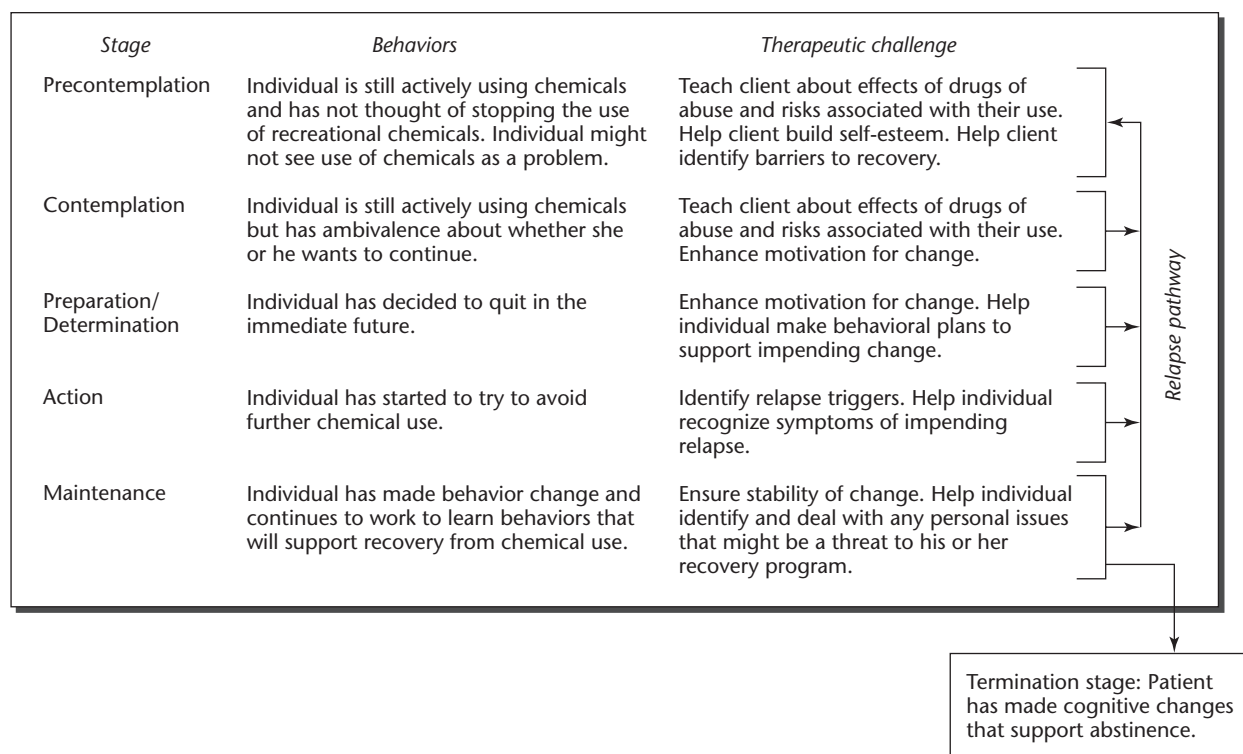


FIGURE 32-1 The Stages of Recovery.

SOURCE: Based on Prochaska (1998) and Prochaska et al. (1992).

abstinence, his or her continued substance use is viewed as presenting more reasons to continue to engage in substance use than consequences. The challenge for the substance rehabilitation professional working with a client in this stage of the change process is to (a) teach him or her the negative effects of substance use, (b) alert him or her to the dangers of continued substance use, (c) address the client's ambivalence to change, (d) help the client envision an alternative lifestyle, (e) help the client to identify barriers that might block this attempt at a lifestyle change, and (f) help enhance the client's self-esteem so that she or he will believe that a lifestyle change is possible (Blume, 2005; Ramsay & Newman, 2000; Rose, 2001)—in other words, to spark the readiness to change that Mintz (2011) identified as the most important factor in psychiatric treatment.

It is important for rehabilitation center staff to avoid focusing on behavioral change issues at this point, as the client still does not view his or her substance use disorder as being a major problem (Connors et al., 2001). The main emphasis of treatment at this stage should be to help clients think about an alternative (drug-free) lifestyle. It is during this stage that defense mechanisms such as denial and rationalization are most prominent (Ramsay & Newman, 2000). If the client is in treatment under external pressure, he or she might attempt to use compliance as a defense against actual lifestyle

change (Blume, 2005), an issue that must be identified and addressed for meaningful behavioral change to occur.

It is only during the stage of **contemplation** that individuals begin to entertain vague thoughts of stopping alcohol or drug use “one of these days.” There is no firm date set for quitting, although the client is actively thinking about quitting at some point within the next 6 months. However, the individual remains ambivalent about change while simultaneously experiencing a growing sense of dissatisfaction with his or her present lifestyle. The person at this stage experiences a love-hate relationship with change, and if they are in doubt about the benefits of cessation they opt not to change (Prochaska, 2011; Prochaska et al., 2013). The individual might remain in this stage for months or years. The client is not working toward recovery during this phase, although he or she might begin to engage in preliminary action that moves them closer to actively attempting to change. For example, the three-packs-a-day cigarette smoker might slowly reduce cigarette consumption to a pack a day in anticipation of eventually quitting.

For the professional working with a client in the contemplative stage, the challenge is to (a) enhance motivation to change, (b) awaken within the client a desire for spiritual growth,² and (c) help the client make a firm decision to change.

²See Chapter 27.

It is not uncommon for a client during this stage to express amazement at how much his or her SUD has impacted the family, for example. A man with an AUD might, after adding up the combined costs of medical treatment, court fines, lost employment, and the physical cost of the alcohol consumed, discover that his alcohol use disorder has resulted in a financial loss that totals well into six digits. “My God, I drank [the equivalent of the purchase price of] a house,” a hypothetical client might exclaim after adding up the accumulated costs incurred by his alcohol use disorder. Another technique that often works is to develop a worksheet on which the pros of continued substance use are compared with the negative consequences of continued substance use.

The next stage is the stage of **preparation**. The client is now ready to change his or her attitude and behavior(s), usually within the next month, and might even have made the initial steps in the change process (Connors et al., 2001; Prochaska et al., 2013). The therapeutic goal during this stage is for the professional to assist the client in making realistic decisions, and to set realistic goals. Another therapeutic goal is for the professional to address maladaptive thoughts that support continued substance use (“I can keep a bottle in my house for friends, as long as I do not actually use it myself,” for example). A danger is that the client’s unrealistic goals or maladaptive thoughts during this effort will undermine further efforts to change.

During the **action phase**, the client takes concrete steps to modify the identified problem behavior. During this phase, the client implements their behavior change plan, often encountering problems as they identify how the original change plan was flawed. The therapeutic goals during this phase center around (a) optimizing opportunities for individual growth, (b) being alert for signs that the client is experiencing problems, (c) encouraging the client to begin the process of building a substance-free support system, (d) helping the client deal with the emotional roller-coaster experienced during this period, and (e) helping the client be realistic about the pace of their recovery (“I can handle being in a relationship, now,” a hypothetical client might say after only 2 months of abstinence).

If the client is able to abstain from alcohol or drugs for at least 6 months, he or she will enter the **maintenance stage** of recovery. During this phase, the individual develops behaviors supportive of recovery, addressing problem areas ignored during the period of active chemical misuse (employment or marital relationships, for example) and confront personal issues that contributed to or exacerbated the SUD. During this phase, the individual learns how to cope with “using” thoughts or urges to return to chemical use, increasing his or her self-efficacy and belief that he or she can succeed in the behavior change. Increased self-efficacy at the end of the first year of

abstinence, including a lower number of days in which alcohol was consumed and smaller amounts of alcohol consumed per drinking day, appears to be a predictor of abstinence at the end of a 3-year period of time (Maisto, Clifford, Stout, & Davis, 2008). The therapeutic challenge during this stage is for the professional to function as a substitute parent, mentor, cheering section, and guide for the client to ensure the stability of change and identify issues that might undermine his or her recovery program.

The maintenance stage can last up to 5 years, after which the **termination stage** is said to begin (Prochaska et al., 2013). This stage is identified as one of “zero temptation and 100 percent self-efficacy” (Prochaska et al., 2013, p. 101). It may actually be that many remain in the maintenance stage for life, given continual temptations to relapse (Prochaska et al., 2013).

Relapse³ is an ever-present danger. In years past this was viewed as a “treatment failure” by many health care professionals. This view has been challenged on the grounds that the addictions are chronic, relapsing disorders similar to cancer, diabetes, or hypertension (McLellan, 2015). Most certainly, a patient who failed to get his or her blood pressure under control after a trial of one hypertensive medication would not be classified as a “treatment failure,” and some diabetic patients are “brittle,” requiring repeated hospitalizations for stabilization and treatment planning, and yet they are not called treatment failures. It has been argued that the same reasoning should apply to the treatment of the substance use disorders.

Recovery from the SUDs is a dynamic process that will often move through the various stages of change in a cyclical rather than a linear manner (Connors et al., 2001; Prochaska, 1998, 2002). The comparison to how patients work through the stages of grief might not be inappropriate here. In both cases the client will be very vulnerable to internal and external cues that reawaken old thought patterns. The individual in recovery from smoking cigarettes might, upon smelling cigarette smoke, start to think about how nice it was to sneak out of the office at a certain time of the day to have a cigarette. The recently bereaved person might, upon hearing a song once shared with a loved one, find him- or herself mired in the pain and misery of mourning his or her lost partner again.

This is one of the more frustrating aspects of substance rehabilitation. The client might make a step forward, then fall back two steps. Over time, she or he might again reach the point where he or she took the step forward, and this time progress yet another step forward. A comparison with

³Discussed in more detail in Chapter 34.

recovery from nicotine use disorder is not out of place here. Periods of smoking abstinence are intermixed with periods of active smoking, which hopefully will become less frequent and shorter in duration as the person learns to live without cigarettes. This is not to say that rehabilitation professionals should accept continued substance use as being unavoidable. Rather, this is to say that the process of recovery from an SUD differs from one individual to the next, and that relapse is a constant danger against which both the client and the professional must be on guard.

One motivational factor against relapse is the client's assessment of the alternatives to continued substance use (Heyman, 2009). Clients will reassess the benefits and consequences of abstinence differently at each stage of the recovery process (Cunningham, Sobell, Gavin, Sobell, & Breslin, 1997). If a client's assessment that the benefits of abstinence do not outweigh the perceived benefits of continued substance use, that person is unlikely to abstain from alcohol or illicit drugs. The treatment professional must therefore continually reassess the client's perception of the benefits and consequences of continued substance use throughout the rehabilitation process. Another goal of the rehabilitation professional is to enhance the individual's belief in his or her ability to make major changes in life⁴ such as learning how to abstain from drugs or alcohol.

The model originally suggested by Prochaska and colleagues (1992) appears to apply both to those individuals who seek professional assistance in learning how to abstain from chemicals and to those who recover from an SUD without professional assistance. Upon reflection, this makes sense, since "natural" recovery from substance use disorders is the norm rather than the exception (Bennett & Golub, 2012; Heyman, 2009; Walters, Rotgers, Saunders, Wilkinson, & Towers, 2003). Both "natural" and "assisted" recovery work toward the same goal: abstinence from substance misuse. It is only logical that they would follow the same process and similar steps to reach that common goal.

Nowinski (2003) suggested an alternative model of recovery to the model suggested by Prochaska and colleagues. The first stage of the Nowinski (2003, 2012) model is that of *acceptance*. This might be achieved either by the individual reaching the decision that the consequences of further substance misuse outweigh the perceived benefits, or through participation in a self-help group such as Alcoholics Anonymous.⁵ If professional assistance is utilized to help

the individual recover from his or her SUD, the patient has the option of utilizing either outpatient or inpatient rehabilitation programs. The goal of all these programs during this stage is the same: to assist the client in accepting the reality of his or her SUD, and the pain and harm caused by this disorder. It is also imperative that the client understand that willpower alone will not guarantee abstinence from alcohol or drugs. Indeed, this belief may be utilized to avoid actual acceptance of the individual's SUD. "I can deal with it on my own" is a common refrain heard by health care professionals working with individuals who misuse substances, "I just need to apply myself to not use again."

It is not until the individual has reached the second stage of recovery in the Nowinski (2003, 2012) model, that of *surrender*, that he or she becomes willing to begin to make the lifestyle changes necessary to support recovery. This is often a difficult step for individuals who misuse alcohol or drugs to achieve. Because of their denial, they tend to believe that they have an inordinate amount of control, not only over themselves, but also over their substance use disorder, and surrender does not come easily to one who is in charge of one's life, now does it? During this stage, the substance rehabilitation professional works to help the client recognize the impact of his or her SUD on both self and others, and to learn how to accept powerlessness as a step toward recovery. This is not always an easy process, even if the client is well motivated. It is much more difficult to accomplish when the client is unmotivated to recognize, accept, or change unhealthy behaviors in their lives.

Reactions to Stage Models of Recovery

The stage models of recovery outlined above have not met with universal acceptance. This is to be expected, since few new theoretical constructs are accepted without criticism, review, modification, and possibly extensive revision. In the field of psychology, stage models tend to pass through several stages before final acceptance: (1) a phase of uncritical acceptance following the introduction of the new model; (2) after a short period of time, guarded criticism is offered about possible problems with the new theoretical model; (3) the criticism increases in volume and frequency until the model is awash in a sea of hostility; (4) the model is relegated to the archives or textbooks as an illustration of the process under consideration, since not every person progresses through each step in the same order as originally postulated. Finally, (5) the model is accepted as a general outline of a process within which there is individual variation. To use an analogy, comparison to the reaction to Albert Einstein's original paper on the theory of relativity in 1905 might not be entirely inappropriate here. His theory was scorned because he was only

⁴"Regulate" can also mean "abstain from the use of," as abstinence is a form of self-regulation. This does not mean that the confidence in one's ability to change is the only element of recovery from an SUD. However, such recovery is unlikely if the individual does not believe that it is possible.

⁵Discussed further in Chapter 35.

a patent clerk in Switzerland who had the audacity to think that he could solve this vexing problem, and only a few people in the field of theoretical physics initially tried to understand his theory. However, with the passage of time, it received greater acceptance and is now the theoretical solution to the problem of how matter and energy are related to each other.

In the field of substance rehabilitation, stage models such as those discussed in this text are often viewed as holy gospel. In reality, such models are “at best descriptive rather than explanatory” (Davidson, 1998, p. 32). One person might remain in a given stage of recovery for months or even years. Another person might make rapid progress through that same stage in a matter of weeks. It is not that the model of change is incorrect, but rather that it is a reflection of the *average* individual’s progression down the path to recovery. Each individual follows his or her own path.

While the stages of change model suggested by Prochaska (Prochaska et al., 1992) has an elegant beauty suggesting that it is accurate and true, research is needed to continue investigating its accuracy and application. Gossop, Steward, and Marsden (2007) found, for example, that while patients had improved in the year following discharge from treatment, there was little correlation between their progress and the various measures of readiness to change. Indeed, it was found that those patients with the highest measured levels of readiness to change were also the same persons who tended to be using the highest levels of heroin at the end of the 1-year follow-up period! This may reflect a greater measure of desperation on the part of heroin addicts who were unable to change, or it might indicate that the current stage models of change are not applicable to every form of SUD. Norcross and colleagues (2011) call for further research to investigate how the stages can be matched with treatments to better serve clients.

Then What Works in Predicting Recovery from SUDs?

One of the most frustrating tenets of substance rehabilitation work is the expectation that those persons in treatment for the misuse of a compound(s) are automatically the same as those who are not in a rehabilitation program. This bias has distorted both clinical research and the development of rehabilitation models, since it ignores the fact that many, perhaps a majority, of those persons with a substance use disorder never seek professional assistance for their SUD (Heyman, 2009). Clinical research has demonstrated that almost 50% of those persons who met the diagnostic criteria for substance dependence did not report even one sign of a current SUD in the past 12 months by the age of 24, and that by the age of 37 this figure had increased to 75% (Heyman, 2009)!

This raises an interesting problem: We do not know enough about what factors predict recovery from a substance use disorder, mainly because only a minority of those persons with a substance use disorder actually are ever admitted to a treatment program. Those persons admitted to a rehabilitation program are possibly the *least likely* to be able to discontinue their substance use (Heyman, 2009). Generalizations from those persons in a substance rehabilitation program to *all* persons with a substance use disorder might be ill advised. We simply do not know how to answer the question posed at the start of this section.

With that caveat in mind, it is possible to tentatively state that there are a multitude of factors that interact to support, or detract from, the individual’s recovery efforts. It has been found, for example, that “ongoing environmental factors can augment or nullify the short-term influence of an intervention [program]” (Moos, 2003, p. 3). Many of these factors, such as a spouse misusing substances, for example, simply lie outside the counselor’s control. Unfortunately, many substance rehabilitation professionals overestimate the impact that their treatment program might have on a given client. It has been found that “relatively stable factors in people’s lives, such as informal help and ongoing social resources, tend to play a more enduring role” (Moos, 2003, p. 3) in assisting the person’s recovery efforts. Treatment might best be envisioned as the foundation for a recovery program, not that it will turn the client’s life around and save her or him from utter destruction.

The foundation on which a client’s recovery might be established appear to involve issues such as:

- Interpersonal relationships:* Individuals who drink more have been found to have few interpersonal resources to draw upon for support.
- Cognitive reappraisals:* Many former drinkers report that their realization that alcohol was causing physical, emotional, and financial damage to their lives was the point where they decided to stop drinking.
- Demographic variables:* Individuals who drink more tend to come from lower socioeconomic groups, which may then provide fewer social supports necessary for recovery.
- Severity of the SUD:* Physical problems, health issues, or legal problems may serve as warning signs that the individual has started to reach problematic levels of substance use.
- Involvement in AA or religious groups* may help the individual better understand the damage that their SUD has caused, while providing social support for recovery.
- Individual expectations and self-evaluation* will help to shape the individual’s perception of recovery,

his or her perception of barriers to recovery, and self-concept issues that might assist or undermine recovery efforts.

A further factor that should be considered is the congruence between the individual's expectations and goals and those of the professional. A client who wishes to attempt to be a "social drinker" might not be willing to participate in a rehabilitation program with a counselor who insists that abstinence is the only possible outcome for therapy. Individuals who do not view themselves as being capable of abstaining from a chemical(s), or who utilized a drug(s) to make themselves numb to feelings of low self-esteem or trauma might have trouble in a recovery program until these issues are adequately addressed. There are so many variables that can influence a given individual's recovery program that only general statements about the "path to recovery" can be made.

Should Abstinence Be the Goal of Treatment?

This question is fiercely debated. Clients often do not wish to abstain from substance use but just learn how to *control* it. Rehabilitation professionals often hold that abstinence is the more appropriate goal, thus establishing the grounds for a goal conflict from the outset of treatment. Yet there are reasons why abstinence should be the appropriate goal, in spite of the client's wishes or hopes. Abstinence from alcohol or illicit drugs reduces the possibility of interpersonal conflict, health care problems, and the financial strain inherent in purchasing a drug(s) of misuse.

Thus, rehabilitation centers focus on total abstinence from alcohol and/or drugs as the goal of treatment. However, there are age differences in the willingness to accept abstinence as a treatment goal. The team of Dawson, Goldstein, and Grant (2007) found, for example, that for persons over the age of 25, abstinence appeared to be the superior goal and yielded the highest success rates. For persons under the age of 25, abstinence-based goals did not appear to improve the success rate for treatment, for reasons that could not be determined from their data. This is consistent with the observations of George E. Vaillant (1995, 1996; Vaillant & Hiller-Sturmhofel, 1996), who, in his work with individuals with AUDs, found that rather than maintaining abstinence, the participants in his studies tended to alternate between periods of abstinence and more or less problematic drinking.

These findings raise interesting questions about the appropriate goal(s) of treatment. Most treatment centers advocate total abstinence as the only acceptable outcome, a goal that is achieved and maintained only by a small percentage of those who enter substance rehabilitation program. Client

abstinence (usually at 3, 6, or 12 months following discharge from rehabilitation) is usually the criterion by which success or failure of a rehabilitation program is measured. However, such assessments are commonly based on patient self-report, and the outcome of the study reflects more the ideology of the assessor than the results of sound scientific research (Muir, 2008). Thus, should total abstinence be a goal for a client who does not share this objective? If so, how should this goal be introduced to the client in a manner that does not immediately cause resistance? The approach suggested by McLellan (2008, 2015) of accepting rehabilitation as a form of disease management, similar to how physicians attempt to control diabetes or hypertension, is more appropriate.

Specific Points to Address in Substance Rehabilitation

During the rehabilitation process, there are a wide range of issues that must be resolved to successfully work with the client with an SUD. First, is total abstinence an appropriate goal? What variables contribute to the individual's substance use that might interfere with efforts to abstain from chemicals? What is the individual's level of motivation, and what form of substance rehabilitation should be initiated? The answers to these questions vary depending on the substance(s) being misused and the individual misusing those compounds. What follows is a very brief summary of some of the more pertinent points to address for a person misusing different compounds.

Alcohol

Substance rehabilitation professionals need to work with clients to identify (1) the consequences of their AUD, (2) its impact on not only themselves but also on their families and significant others, (3) whether they thought abstinence was a worthy goal in light of this understanding, and (4) what factors motivated the individual's use of alcohol or might serve as a barrier to recovery. A client who states, "I am only here to please my probation officer" has identified a significant barrier to recovery (no desire to do more than achieve a degree of impression management), for example. The professional in this case must assist the client in internalizing a desire to change for personal reasons, not because of external pressure.

A significant problem that asserts itself not only with alcohol but with all of the substances of misuse is the illusion of control. A client might go into a bar and drink only soda for the evening while on "pass," and then claim that she or he has achieved the ability to control his or her desire to drink and thus is ready to graduate from treatment. Usually, these

individuals are on the brink of a major relapse. A variation is the individual who will have one or two beers on one occasion without suffering any adverse consequences. Because they did not suffer any consequences on this one occasion, it is possible that they will dismiss everything that they learned while in treatment as not applying to them, setting the stage for an ultimate relapse.

Narcotic Analgesics

The goal of abstinence for a person addicted to a narcotic analgesic depends on the length of time the person has been addicted, and his or her motivation for a drug-free lifestyle. A person who has only recently become addicted to a narcotic and who is highly motivated to abstain will present a different clinical picture than the person who has been addicted to narcotics for the past 10 years, and who is only interested in a methadone maintenance program.⁶ Simple detoxification from narcotics is not the answer: Ninety percent of those opioid-dependent persons who complete a detox program return to the misuse of chemicals within 6 months (Schuckit, 2006a, 2006b).

A set of research studies under the direction of Hser supported a pessimistic outcome for OUD (Hser, Anglin, & Powers, 1993; Hser, Evans, Grella, Ling, & Anglin, 2015; Hser, Hoffman, Grella, & Anglin, 2001). The authors of these studies followed a group of opioid-dependent individuals who had been arrested in California, and 24 years after their initial assessment it was found that only 22% of the original sample of 581 individuals were opiate-free (Hser et al., 1993). An additional 7% of the original research sample were on a methadone maintenance program, and 10% reported just occasional episodes of narcotics abuse. Unfortunately, almost 28% of the original sample had died in the 20-year period between their initial arrest and the 24-year follow-up, with the causes of death being homicide, suicide, and accidents, in that order.

At the time of the 34-year follow up, almost half of the original sample of 581 individuals were found to have died (Hser et al., 2001). This was almost equal to the number of original subjects who were opioid-free, as confirmed by urine toxicology testing, and an additional 10% of the original subjects refused to submit to urine toxicology testing. The authors concluded that heroin misuse patterns were “remarkably stable” (p. 503) over the course of the study, with some subjects relapsing back to active opioid dependence after as much as 15 years of abstinence. The authors suggested that heroin addiction was a lifelong condition, with severe social and medical consequences. However, it should also be noted that the Hser and colleagues, (2001) study found that

a significant percentage of their original research sample were opioid-free, a finding consistent with other studies that have found that more than one-third of opioid-dependent persons will eventually achieve a drug-free lifestyle. This opioid-free lifestyle is usually only achieved around 9 years after the individual first became addicted to opioids (Jaffe, 2000).

The newer research by Hser and colleagues (2015) supports the chronic-relapsing view of OUDs. They found that longer episodes of treatment do point toward better outcomes, yet the mortality rate for those with OUDs is up to 20 times greater than for typical individuals, with overdose being the most frequent cause of death. For those who survive, having 5 years of abstinence increases the potential of continuing abstinence in the future, yet the likelihood of stable abstinence is less than 30% for those followed between 10 and 30 years.

At this point in time, there are opioid agonist replacement therapies⁷ that, while not being perfect solutions to the problem of narcotics addiction, at least offer the promise of helping individuals to control their craving for opioids while they address other life issues. Further, as research has demonstrated, approximately one-third of opioid-dependent persons will eventually become free of narcotics after an extended struggle with their SUD. Thus, the question of whether abstinence or opioid agonist therapy is the goal of treatment should be a joint decision between the professional (or therapeutic team) and the client.

CNS Stimulants

Traditionally, addiction to the CNS stimulants was not in itself grounds for admission to an inpatient detox facility. One exception to this is the possibility that the individual has one of a number of medical complications caused or exacerbated by the misuse of CNS stimulants that may prove to be life-threatening unless the individual were to be monitored by health care professionals during the withdrawal process. Another exception is when the patient is also addicted to compounds such as alcohol, where withdrawal can potentially be life-threatening. Yet a third exception to the rule is when the individual has developed a suicidal depression as a result of CNS stimulant withdrawal. A qualified health care professional should assess each client, keeping in mind that the client's state of mind, past history of suicidal thinking or attempts, current medical status, support systems, and history of success or failure at past detoxification attempts all help to determine the client's specific need for a given level of care.

CNS stimulant withdrawal proceeds through both an acute and an extended withdrawal phase. Some of

⁶Discussed in Chapter 33.

⁷Discussed in Chapter 33.

the emotional and physical problems experienced during both the acute and extended withdrawal phases may serve as relapse triggers for the client, and thus must be addressed by the attending health care staff. However, available evidence suggests that for those individuals who are able to remain abstinent from CNS stimulants such as cocaine for 12 weeks, up to 80% will remain drug-free for the first 6 months following treatment. But, as will be discussed in Chapter 34, even persons with extended periods of abstinence will find themselves suddenly experiencing periods of craving for CNS stimulants, usually in response to external stimuli associated with past substance use (songs, smells, physical appearance of a person seen in passing, etc.)

One very real problem in working with the individual who misuses CNS stimulants is that the individual often has forgotten what a drug-free lifestyle is like. This underscores the need for relapse prevention training as well as social support groups such as Alcoholics Anonymous, Narcotics Anonymous, Cocaine Anonymous, or one of the emerging faith-based support groups.

Marijuana

Although it has been estimated that only 10% of those who misuse marijuana eventually become addicted to it, marijuana addiction is still a very real phenomenon. It is difficult to convince adolescents or young adults of this danger and it is rare for a person with an SUD to misuse *only* marijuana. Further, it is rare for a person who is addicted to marijuana to present for treatment, unless there is some form of external coercion.

Total abstinence from all drugs of misuse is thought to be imperative when working with the individual with a cannabis use disorder (Smith, 2001). Compounds that cause any of the psychoactive effects of marijuana would reawaken memories of marijuana use, and thus serve as a relapse “trigger.” Further, since many individuals use marijuana as a way of coping with negative feelings, rehabilitation professionals must help the client learn non-drug-centered coping mechanisms for these negative feelings. A complete assessment of the client’s motivation for marijuana use, and the development of alternative coping mechanisms for these problems, is imperative. Ancillary support services such as community-based support groups are also of value.

Anabolic Steroids

It is important to keep in mind that the individual’s motivation to misuse anabolic steroids is rarely the same as

that seen in other individuals misusing substances. The individual’s motivation for misusing these compounds will need to be identified. For example, the individual misusing anabolic steroids who believes that these compounds will enhance their physical appearance will present with a different motivation than the individual who wishes to build muscle strength.

Medical supervision of the individual misusing anabolic steroids is mandatory. The physician can order blood and urine tests that, while they do not directly indicate anabolic steroid misuse, do strongly hint that the patient has continued to use these compounds. The physician is also in the best position to confront the anabolic steroid user, who might otherwise dismiss a substance rehabilitation professional’s attempts at intervention with a wall of denial and medical jargon that the counselor is ill prepared to refute. The physician, on the other hand, can identify specific test results that warn of cardiac, liver, or other organ damage induced by the misuse of these compounds, and dismiss the client’s semi-informed rationalizations of harmlessness with the facts.

A very real problem in working with individuals misusing anabolic steroids is that many of the complications caused (or exacerbated) by these compounds do not appear until years after the individual starts to use them. A high school football player, for example, will often dismiss warnings that anabolic steroids can exacerbate the build-up of atherosclerotic plaque. These problems are decades away, at least in their opinion, and winning is everything, is it not? As was discussed in the chapter on child and adolescent substance use disorders, adolescents (and young adults) do not process information about the dangers associated with substance use in the same manner that older adults do, and the substance rehabilitation professional needs to keep this in mind when working with an individual using steroids.

The client’s motivation for using steroids should be identified, and coexisting disorders (such as body image problems) should be identified and addressed. Proper nutritional guidance will often prove to be a valuable adjunct to rehabilitation as the client learns that he or she can achieve many of the same desired effects without the use of steroids. Group therapy with others recovering from anabolic steroid use may prove to be of value. Community-based support groups may also prove useful, but there are very few such support groups devoted only to individuals who have misused anabolic steroids.

Hallucinogens

Individuals who misuse hallucinogens rarely have the same motivation as do those persons who misuse alcohol or

narcotics. While many of these compounds may induce a sense of euphoria, individuals who use hallucinogens tend to point to their desire to induce sensory distortions. This is often done by persons who believe that they are more creative when under the influence of these compounds, which is a source of motivation that is virtually never seen in those misusing narcotic analgesics, for example. While the potential dangers of hallucinogen use are limited,⁸ the use of these compounds does impact psychosocial functioning, and it is illegal, and these are factors that the rehabilitation center staff might wish to emphasize in working with clients who use these compounds.

Reactions to the Concept of Addictions Treatment

The process of substance rehabilitation has not met with universal acceptance. Churchland (2013) argued, for example, that science has failed to develop a treatment format that defines “success” in a scientifically verifiable manner that can be replicated across studies. Further, many treatment centers or their staff are reluctant to adopt new treatment methods or techniques that have been demonstrated to be more rapid and possibly more effective (Hunter, Ober, Paddock, Hunt, & Levan, 2014; Icro, Maremmanni, Lubrano, Nardini, Dell’Osso, & Pacini, 2014). All too often the outcome of this process is that the individual who relapses is placed in either the same or a similar rehabilitation facility that uses techniques that have been demonstrated to

be ineffective for that person, who is then labeled as being treatment-resistant.

Chapter Summary

In this chapter, two different stage models of the recovery process were identified and discussed. The most popular model was introduced by Prochaska and colleagues (1992). This model suggests that while progress is not linear, individuals who wish to make behavioral change(s) move from a precontemplation period, in which no behavioral change is being considered, into a phase where the individual is starting to consider the possibility of a behavioral change, known as contemplation. The individual may remain in this stage for a number of months, or even years, thinking about the possibility of attempting a major behavioral phase “one of these days,” but without firm plans to do so starting on a specific date.

Individuals in the contemplation phase struggle with a vague sense of dissatisfaction with their present life circumstances. It is during the action phase that the person attempts to make the behavioral change(s) being contemplated. After achieving a substance-free lifestyle for at least 6 months, the individual enters the maintenance phase, working to identify and develop behavior(s) that will assist in maintaining the behavioral change(s) achieved to date. The maintenance phase blends into the termination phase after about 5 years of abstinence.

Also discussed were some of the factors that might support the individual’s attempt at abstinence, and factors specific to different classes of drugs of misuse that rehabilitation professionals must consider in working with clients misusing those compounds.

⁸MDMA’s effects on memory being an exception to this rule.

Pharmacological Interventions for Substance Use Disorders¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 33.1** Understand the theory behind the use of pharmacotherapy for SUDs
- 33.2** Identify the commonly used pharmacological treatments for alcohol use disorders
- 33.3** Identify the commonly used pharmacological treatments for stimulant use disorders
- 33.4** Identify the commonly used pharmacological treatments for cocaine use disorders
- 33.5** Identify the commonly used pharmacological treatments for opioid use disorders
- 33.6** Identify the commonly used pharmacological treatments for tobacco use disorders

Introduction

Pharmacotherapy, or the utilization of select pharmaceuticals to treat a specific condition, often is also often employed in the treatment of the substance use disorders. Thankfully, there have been recent advances in pharmacological options for SUDs (Sherman, Hartwell, McRae-Clark, & Brady, 2017). However, most of the pharmaceutical agents currently in use to treat the SUDs are compounds originally developed to treat other conditions, and were found by chance to also be useful as adjuncts to treating the SUDs (Ciraulo, 2004). The use of these compounds in substance rehabilitation programs is often classified as “off-label” applications, which have not been adequately examined by the pharmaceuticals company and which leave the prescribing health care provider vulnerable to malpractice suits should there be an unfortunate outcome when such compounds are used. Pharmacological interventions continue to be underutilized for treating SUDs (Sherman et al., 2017). It is imperative that health care professionals have a working knowledge of some of the more common pharmacological interventions used to treat substance use disorders, their original intended purpose, and how they are being used off-label to help physicians treat persons with SUDs.

¹The information provided in this chapter, like the information provided in the rest of this text, is intended to illustrate the manner in which certain medications are used by physicians to treat illicit drug use. It is neither intended, nor should it be used, as a guide for the treatment of any given individual(s).

The Theory Behind Pharmacotherapy of SUDs

Lukas (2006) identified several subgroups of medications that might be utilized as adjunctive treatments for SUDs: (1) medications that control withdrawal symptoms, (2) medications that control the individual's craving for drugs, (3) aversive agents that cause dysphoria when certain compounds are used, (4) compounds used to treat concurrent psychiatric disorders, (5) agonist compounds used in certain maintenance programs, and (6) medications used to treat drug overdoses. Only minimal discussion of the fourth category of compounds, psychopharmaceuticals used to treat mental illness, will be included in this text.² All medications discussed in this chapter fall into one or more of the categories suggested by Lukas (2006). A very real danger in using pharmaceuticals to treat substance use disorders is that the patient will become "enamored" (Washton & Zweben, 2006, p. 103) with pills. Their use might thus be, for at least some who misuse substances, an extension of their "addictive thinking" rather than an adjunct to treatment. Finally, not every patient will require pharmaceutical support for their recovery program, while others will reject such adjunctive aids (Harris, Kivlahan, Bowe, & Humphreys, 2010). So, while pharmacotherapy is often useful, it is not a panacea for the substance use disorders, and often is unwanted by the patient.

Pharmacological Treatment of Alcohol Use Disorders

There are two subcategories of medications used in the treatment of alcohol use disorders (AUDs): (1) those medications used to control the symptoms of the alcohol withdrawal syndrome and (2) those used in relapse prevention, including aversive agents that cause dysphoria when the individual ingests alcohol. We will begin our discussion with the medications used to control the alcohol withdrawal syndrome.

Pharmaceutical Treatment of the Alcohol Withdrawal Syndrome (AWS)

Currently, the benzodiazepines are accepted as the treatment of choice for controlling the symptoms of the AWS (Bayard, McIntyre, Hill, & Woodside, 2004; Daeppen et al., 2002;

Mariani & Levin, 2004; McKay, Koranda, & Axen, 2004; Sherman et al., 2017). Physicians use these medications to first control the withdrawal symptoms, and then to safely taper the dose down over a period of time so that the patient avoids most of the discomfort and risks associated with the AWS. The intermediate or long-acting benzodiazepines are the compounds of choice, as they avoid the danger of "rebound" withdrawal symptoms caused by between-dose variations in the blood benzodiazepine levels. Some physicians advocate the use of diazepam,³ chlordiazepoxide, lorazepam, or chlordiazepoxide, depending on the patient's risk factors, to control the AWS (Sherman et al., 2017).

However, there is a minor controversy about how the benzodiazepines should be employed for the control of alcohol withdrawal symptoms. Some physicians advocate a **fixed-dosing regimen**, in which a specified amount of the selected benzodiazepine is administered on a schedule, such as an oral dose of 50–100 mg of chlordiazepoxide every 6 hours, with an additional dose of 25–100 mg administered every hour until the withdrawal symptoms are controlled. Then over a period of days the dosage level is reduced until the patient is medication-free. If diazepam is used, the dosage level is usually between 5 and 20 mg every 6 hours until the symptoms are controlled, although in an extreme case a daily accumulated dose of 2,000 mg a day might be necessary to control the AWS (Bayard et al., 2004). *Loading dosage* is another regimen used, in which long-acting benzodiazepines are given every 2 hours, then tapered (Sherman et al., 2017).

Most physicians now advocate a symptom-driven approach to the pharmacological treatment of the AWS, often called a **symptom-triggered regimen** (McKay et al., 2004; Sherman et al., 2017). Symptom-driven withdrawal programs allow for the dose to be adjusted depending on the patient's observed symptoms, resulting in significantly lower daily total benzodiazepine dosage levels (Bayard et al., 2004; Spiegel, Kumari, & Petri, 2012). If the patient should experience higher levels of agitation or hallucinations, a low dose of an antipsychotic medication such as haloperidol can be added to the patient's regimen to further augment the pharmacological support being offered to the patient (Bayard et al., 2004). Unfortunately, benzodiazepine-induced disinhibition might be mistaken for alcohol-withdrawal disinhibition, resulting in larger doses of the very medications that caused (or at least exacerbated) the disinhibitory behaviors in the first place being administered to the patient. Ultimately, all three regimens may be appropriate, depending on the setting within which they are used, and most tapers end within a week (Sherman et al., 2017).

²There are a number of psychiatric textbooks that provide excellent discussions of how these compounds are applied to the treatment of mental illness, and if interested in learning more about these compounds, the reader is advised to seek information through these sources.

³The benzodiazepines are discussed in more detail in Chapter 7.

There is some research evidence suggesting that the anticonvulsant medications such as gabapentin and carbamazepine might be a safe alternative to use in treating mild to moderate-intensity AWS (Sherman et al., 2017). Advantages of such medications are that they reduce the individual's craving for alcohol during the withdrawal process, reduce seizure likelihood, and are generally not substances that have misuse potential (Sherman et al., 2017).

Addolorato and colleagues (2007) suggested that the compound *baclofen* might be useful both during the acute withdrawal phase and during the post-withdrawal phase since it appears to lower the individual's craving for alcohol during this period. There is ongoing research both to replicate the original findings and to determine the correct dosage level to offer the greatest benefit to the patient.

Pharmacological Treatment of the Alcohol Use Disorders

In spite of the terrible damage wrought by the alcohol use disorders (AUDs), it is surprising to learn that only a minority of persons with an identified alcohol use disorder receive pharmacological support for their efforts to abstain from alcohol (Harris et al., 2010). There are five groups of medications considered for the treatment of the AUDs (Sherman et al., 2017): (a) alcohol-sensitizing, (b) opioid antagonists, (c) anti-craving, (d) anti-seizure, and (e) serotonin antagonists. It should be noted that there are no criteria to identify those persons who would benefit most from pharmacological treatment(s), or which medication would be best for an individual with an AUD (Aldhous, 2010).

FDA approval has been given for disulfiram, naltrexone, and acamprosate (Sherman et al., 2017). Other compounds being used to treat the AUDs are either being tried “off-label”⁴ or are being investigated as possible agents to use in treating AUDs. While these compounds have met with limited success, there are a number of research programs under way to identify new compounds that might be of value in treating the alcohol use disorders. We will discuss some of the compounds most commonly used in the treatment of alcohol dependence below.

DISULFIRAM

At the 1949 annual meeting of the American Psychiatric Association, the team of Barrera, Osinski, and Davidoff (1949/1994) presented a paper in which the medication Antabuse[®] (disulfiram⁵) was said to be useful as an

antidipsotrophic⁶ compound. The compound would cause “unpleasant effects” when mixed with alcohol, and as such seemed to show promise in the treatment of alcohol use disorders. These unpleasant effects were discovered quite by accident by workers in rubber factories who were experimenting with disulfiram as a possible way to vulcanize rubber. Many of these workers would stop off for a drink or two after work, only to become violently ill from an unsuspected interaction between the alcohol and the disulfiram ingested through their skin (Bohn, 2001).

A few years later, researchers searching for a way to treat worm infestations in animals administered disulfiram to the animals and then went to have a few drinks with coworkers before going home. Like their counterparts in the rubber industry, they also experienced an unpleasant interaction between the alcohol and the disulfiram that they had inadvertently absorbed through the skin. A veterinarian observed the interaction and suggested that perhaps disulfiram might be useful in treating alcoholism (Bohn, 2001). It was developed as such a medication, and it is the oldest antidipsotrophic medication in use (Sherman, 2008).

Clinically, disulfiram is a **prodrug**^{7,8} that must be biotransformed into another compound before it has the desired effect (Swift, 2010). The metabolite of disulfiram interferes with the biotransformation of alcohol by destroying the enzyme aldehyde dehydrogenase. Aldehyde dehydrogenase is an enzyme that breaks down acetaldehyde, an intermediate metabolite produced during the alcohol biotransformation process. Normally, acetaldehyde is broken down very rapidly in the drinker's body. Without aldehyde dehydrogenase, acetaldehyde, which is about 30 times as toxic to the body as alcohol, builds up in the body, causing discomfort to the drinker (Moalem & Prince, 2007; Sherman et al., 2017). As the acetaldehyde levels increase further and further into the toxic range, the drinker will experience: facial flushing, heart palpitations, a rapid heart rate, difficulty in breathing, nausea, vomiting, and hypotension (Schuckit, 2006a, 2006b; Sofuoglu & Kosten, 2004). *The disulfiram/alcohol reaction can be fatal*, especially in cases where the individual has ingested large amounts of alcohol or is sensitive to the interaction effects of these compounds (Lehne, 2013). This makes immediate medical assessment and treatment necessary to help ensure the individual's survival.

⁶Literally, *anti-dipsomania*, a term popular in the 19th and early 20th centuries for alcoholism. Both terms are obsolete.

⁷See Chapter 3 and the Glossary.

⁸Few people actually are aware of this fact. The compound that it must be biotransformed into is diethyldithiocarbamate methyl diethyldithiocarbamate (Swift, 2010).

⁴See Glossary.

⁵This is the generic name.

Under normal conditions, it takes 3–12 hours after disulfiram is first ingested before it can block the alcohol biotransformation process. Thus, physicians usually prescribe a 3–5-day “loading dose” period, in which the medication is administered daily, to establish a therapeutic blood level of disulfiram in the patient’s blood. When a patient whose disulfiram level has reached that therapeutic level ingests alcohol, she or he will usually experience the interaction within about 30 minutes of the time that they first begin to drink. Because of its long half-life, disulfiram is usually administered only two or three times a week after the loading-dose period. On rare occasions, it is administered daily. Disulfiram remains fully effective for 24–48 hours, and in most cases there is no alcohol–disulfiram interaction after 6–7 days, although there are rare reports of such reactions taking place 14 days after the patient’s last use of disulfiram.

The alcohol–disulfiram interaction continues for between 30 and 180 minutes, although there are isolated cases where the interaction has continued for longer than this. Factors that influence the strength of the alcohol–disulfiram interaction include (a) the time that the person has been taking disulfiram, (b) the time since the last dose of disulfiram was ingested, (c) the amount of alcohol ingested, and (d) the individual’s biochemistry. As with any other medication, the biochemistry of some persons is such that their bodies biotransform disulfiram at a more rapid rate than the average person, which will weaken the alcohol–disulfiram effect if they should drink at a time when their blood disulfiram level is lowest.

When used properly, disulfiram was thought to provide an additional source of support for the individual in early abstinence during a moment of weakness, since it takes a number of days for disulfiram to be eliminated from the body. This allows the person time for second thoughts and a possible renewed commitment toward abstinence. To help patients understand the consequences of mixing alcohol with disulfiram, some treatment centers advocate a learning process in which the patient receives a loading dose of disulfiram over the course of several days, and then is allowed to ingest a small amount of alcohol. This will induce the alcohol–disulfiram interaction effect under controlled conditions, in the hopes that the individual will then be less likely to carry out this experiment on their own after discharge from treatment.

Disulfiram, like all pharmaceutical agents, has an extensive list of side effects. Before 1970, megadoses of disulfiram⁹ were used, causing such side effects as delirium, depression, anxiety, and manic and psychotic reactions. The recommended dose of disulfiram has been drastically reduced to only 250–500 mg per dose since then; however, it is not

recommended that patients with diabetes, hypothyroidism, cerebral damage, epilepsy, nephritis, or women who are pregnant use disulfiram (Gitlow, 2007). At the dosage levels currently in use, identified side effects include skin rash, fatigue, halitosis, a rare and potentially deadly form of hepatitis, peripheral neuropathies, hallucinations, and potential damage to the optic nerve (Schuckit, 2006a, 2006b; Tekin & Cummings, 2003). There are also indications that it may exacerbate the symptoms of schizophrenia, and may interfere with male sexual performance. Further, disulfiram is not recommended for elderly patients because it may contribute to possible cardiovascular problems (Drew, Wilkins, & Trevisan, 2010; Klimstra & Mahgoub, 2010).

There are a number of potential disulfiram–medication interactions that need to be considered. It potentiates the effects of the anticonvulsant medication phenytoin,¹⁰ and patients with a seizure disorder who take phenytoin should consult with a physician before taking disulfiram to avoid the danger of medication toxicity (“Medication interactions,” 2008). Disulfiram also potentiates the effects of oral anticoagulants, a matter of some concern for patients who are on anticoagulant therapy, as well as the antibiotic isoniazid, used to treat tuberculosis. Its use is contraindicated in patients receiving (or who have recently received) metronidazole, alcohol, or “hidden” alcohol often found in elixirs, certain foods, or aftershave products.

There are many other problems associated with disulfiram use as an adjunct to treatment. Medication compliance is difficult, and only 20% of those prescribed disulfiram take it as prescribed (Myrick & Wright, 2008; Rounsaville, 2006; Virani, Bezchlibnyk-Butler, & Jeffries, 2009). Researchers have attempted to develop disulfiram implants that would provide a long-term supply of medication that could be absorbed over extended periods of time; however, research has failed to demonstrate that these preparations result in any significant increase in abstinence rates over the traditional oral forms (Bohn, 2001). At best, it is thought to be moderately effective (Lehne, 2013) although some researchers have concluded that it is no more effective than a placebo as a support to abstinence (Bohn, 2001; Carroll, 2003; Jonas et al., 2014; Mariani & Levin, 2004; Sherman et al., 2017). This lack of effectiveness may be due, in part, to the fact that disulfiram does not reduce the individual’s craving for alcohol in the early stages of abstinence. Because of its limited effectiveness, and the danger of disulfiram-induced side effects, its use is becoming increasingly rare (Standridge & DeFranco, 2006), although it is technically safe and effective when used under proper supervision (Sherman et al., 2017).

⁹In case you wanted to know, these dosage levels were 1–2 grams per dose (or 1,000 to 2,000 mg per dose).

¹⁰Often sold under the brand name of Dilantin.

NALTREXONE

It has been found that alcohol ingestion causes the release of endogenous opioids within the brain's "pleasure center," especially the mu opioid receptor. It is thus logical to assume that any compound that blocks the mu receptor will reduce the individual's incentive to drink. There is mixed evidence that naltrexone, a mu opioid agonist achieves this effect (Jonas et al., 2014; Mariani & Levin, 2004). Initial expectations for naltrexone as the "magic bullet" that would control urges to relapse has not been supported by subsequent research (Swift, 2010). One study found that 50% of patients on naltrexone relapsed within the first 12 weeks (Kiefer et al., 2003). A number of studies have failed to find *any* benefit from naltrexone in preventing relapse back to active alcohol misuse (Mariani & Levin, 2004). Further, there is evidence of a dose-dependent toxic effect on the liver, limiting its use in patients with some form of liver damage.

There is some evidence suggesting that naltrexone is of limited value in the treatment of a subform of AUDs known as "reward" drinkers. Such individuals crave alcohol, and when they give in to these cravings and drink, they experience a profoundly rewarding experience. Naltrexone blocks the reward cascade, thus reducing the incentive for these individuals to consume alcohol (Myrick & Wright, 2008). This would explain why, although naltrexone does not prevent the initial "slip," it does appear reduce the chance that the slip will become a full-blown relapse (Volpicelli, 2005). There is also evidence suggesting that individuals with a familial history of alcohol use disorders may be more likely to benefit from naltrexone than patients who do not have a familial history of an AUD, although the reason for this effect is not known (Gilman, Bjork, & Hommer, 2007).

Medication compliance with naltrexone is a problem, partially due to side effects such as nausea, headache, anxiety, and sedation. Forty percent of patients prescribed this medication discontinue taking it within 30 days, and 60% do so within 90 days (Carroll, 2003). To address this issue, a time-released form of naltrexone was developed and marketed under the brand name Vivitro® (*Prescribing Information*, 2006). This form of naltrexone is injected once a month, but while it helps to control the craving for alcohol in the early stages of recovery, its high cost prohibits its use by many patients (Garbutt et al., 2005). Although this form of naltrexone seems to be effective in reducing drinking in men, it has not been shown to be effective for women (Sherman et al., 2017).

ACAMPROSATE¹¹

Acamprosate (sold in the United States under the brand name Campral®) has been used by physicians as an aid in the

treatment of alcohol use disorders, in particular as an anti-craving medication, since 1989, with approval by the FDA in 2004 (Hunter & Ochoa, 2006; Sherman et al., 2017). Acamprosate is derived from the amino acid taurine, which itself has effects similar to those of alcohol (Stahl, 2008). It has a half-life of 20–33 hours and requires 5 days to reach full effectiveness (Lehne, 2013). Like alcohol, acamprosate seems to inhibit the glutamate receptors while enhancing GABA receptors. This compound appears to limit the release of glutamate both during and after the period of alcohol withdrawal. This appears to be accomplished through a drug-induced alteration of the calcium channels in neurons, slowing the responsiveness of those neurons to stimulation (Carroll, 2003; Hunter & Ochoa, 2006; Mariani & Levin, 2004; Overman, Teter, & Guthrie, 2003). This action both blocks some of the rewarding actions of alcohol and limits the craving for alcohol reported by many individuals in the early stages of recovery from alcohol dependency (Stahl, 2008).

Acamprosate has a limited side-effect profile, and there is no evidence of a rebound effect when it is discontinued (Hunter & Ochoa, 2006). There has not been evidence of acamprosate misuse. Its safety profile even allows it to be used during acute alcohol withdrawal (Gual & Leher, 2005). There are no reports of drug interactions between acamprosate and other pharmaceuticals, including disulfiram (Overman et al., 2003). Between 10 and 17% of patients started on this medication will experience transient diarrhea, which usually resolves within a few days (Hunter & Ochoa, 2006; Standridge & DeFranco, 2006). Other rare side effects include depression, nausea, drowsiness, dry mouth, and increased sexual desire (Hunter & Ochoa, 2006). It is excreted virtually unchanged by the kidneys (Overman et al., 2003; Sherman, 2008). There is some evidence suggesting that it might improve the quality of sleep during the early stages of recovery (Staner et al., 2006). This is an advantage, since sleep disturbance is a common complaint in patients in the early stages of recovery.

Unfortunately, medication compliance is a problem since this medication must be taken three times a day. Further, the clinical evidence supporting the use of acamprosate is limited, with some studies finding no difference in abstinence rates between those patients who use this pharmacological support and those who do not (Anton et al., 2009; Gitlow, 2007; Swift, 2010). In contrast to this, Jonas and colleagues (2014) concluded that when used as directed, acamprosate was as effective as naltrexone in maintaining abstinence from alcohol use.

The compounds discussed above are those that are approved for the treatment of alcohol use disorders. In the section that follows, we will examine some of the compounds that are thought to be of value, or that are being examined as possible pharmaceutical aids in the recovery from alcohol use disorders.

¹¹The chemical name for this compound is *calcium acetylhomotaurinate*. We will use the term acamprosate as this is the name most commonly used for this compound in the United States.

TOPIRAMATE

This medication was originally introduced for the control of epilepsy. Topiramate enhances the effects of GABA in the brain, blocking the rewarding effects of alcohol and thus the individual's incentive to drink (Jonas et al., 2014; Paparrigopoulos, Tzavellas, Karaikos, Kouriaba, & Llappas, 2011; Sherman et al., 2017). The team of Baltieri, Daro, Ribeiro, and de Andrade (2008) found that 67% of their research sample who were placed on topiramate had remained abstinent at the end of 4 weeks of treatment, 62% remained abstinent at the end of 8 weeks, and 46% were still abstinent at the end of 12 weeks of treatment. All three of these abstinence figures were significantly better than those achieved with naltrexone or a placebo, the authors reported.

It has also been found that patients on topiramate had a significantly lower level of liver enzymes (suggesting abstinence) as compared with those persons who did not receive this medication, and achieved a higher level of function. This might be the mechanism by which topiramate reduces the frequency of alcohol use by those who drink chronically (Johnson et al., 2008; Mariani & Levin, 2004; Rubio, Martinez-Gras, & Manzanares, 2009; Sofuoglu & Kosten, 2004). These studies would suggest that topiramate might be a valuable asset in the pharmacological treatment of alcohol use disorders in younger adults. However, topiramate can induce cognitive impairment in older drinkers and presents other side effects that might make the patient or their physician reluctant to use it (Drew et al., 2010; Shinn & Greenfield, 2010). Given that it has had poor results as compared to other approved medications and also has a number of side effects, its usefulness with AUDs seems limited at present (Sherman et al., 2017).

BACLOFEN

Experimental research suggests a possible value of high doses of baclofen in the treatment of alcohol dependence. Baclofen binds at the GABA-B receptor sites in the brain and is not hepatotoxic (Addolorato et al., 2007). It appears to reduce alcohol withdrawal distress at least as well as diazepam (Addolorato et al., 2008). However, the long-term effectiveness of this compound in treating alcohol dependence is still being explored. The team of Garbutt, Kapmov-Polevoy, Gallop, Kalka-Juhl, and Flannery (2010) failed to find any evidence of positive clinical effect from this compound on persons with an alcohol use disorder. However, their research sample was small, and further research into the possible application of baclofen in the treatment of persons with an AUD needs to be carried out. In contrast to these findings, Muller and colleagues (2015) found that high doses of baclofen did appear to reduce the number of days the volunteers in their research sample consumed alcohol, although a significant percentage of those who started the study dropped out before the study

was completed. Thus, there is a need for more research into the possible applicability of baclofen as an adjunctive treatment to the AUDs.

ARIPIPRAOLE

Aripipraole, an agent used to treat both psychotic disorders as well as the bipolar disorders, has been recommended as an aid in the treatment of the alcohol use disorders (Kranzler et al., 2008). While this medication has been found to reduce alcohol's ability to induce euphoria through its ability to block dopamine receptors, it also increased alcohol-induced sedation in a small study (Kranzler et al., 2008). While the original results were promising, there is a need for additional study into the utility of this compound in treating alcohol use disorders, according to the authors.

NALMEFENE

This is an opioid antagonist similar to naltrexone in terms of its chemical structure (Mason, Salvato, Williams, Ritvo, & Cutler, 1999). However, nalmefene has a longer half-life than does naltrexone, and it also binds more effectively at the mu, kappa, and sigma receptor sites, which are the neurotransmitter receptor sites that are thought to be involved in alcohol-induced euphoria. This would suggest that this compound is at least as effective as naltrexone as a pharmacological support for the treatment of the alcohol use disorders. However, there is mixed support to date, with some research indicating no difference compared to a placebo, whereas other research has found the opposite (Sherman et al., 2017).

BUSPIRONE

Initial research suggested that buspirone might have value as a pharmacological support for the treatment of alcohol use disorders. However, subsequent research has found that buspirone is only of value for individuals who had a preexisting anxiety disorder and who were misusing alcohol as a form of self-medication (Mariani & Levin, 2004).

METRONIDAZOLE

Metronidazole is an antibiotic compound that was considered as a possible adjunct to the treatment of the alcohol use disorders in the 1970s. This medication, when mixed with alcohol, will induce a disulfiram-like response. However, subsequent research has failed to suggest that metronidazole is effective as an **antidipsotrophic**¹² medication (Hester & Squires, 2004).

LITHIUM

In the last decades of the 20th century, there was a great deal of research into the possible use of lithium to treat

¹²See Glossary.

the alcohol use disorders. Lithium is an element that has been found useful in the treatment of the *bipolar affective disorders*.¹³ Early research was promising, but subsequent research failed to replicate the early research evidence, and it is generally assumed that lithium is only of value for those individuals who have a concurrent alcohol use disorder and a bipolar disorder.

ONDANSETRON

This compound has been used to treat early-onset alcoholism in Europe, with some success (Johnson et al., 2000). It is based on the theory that early-onset alcoholism might be the result on a serotonergic system dysfunction. Ondansetron is an experimental 5-HT₃ blocker. The 5-HT₃ receptor site has been found to be involved in the subjective experience of alcohol-induced pleasure. By blocking this receptor subtype, it would be possible to reduce the individual's incentive to use alcohol, since the individual would derive no pleasure from the alcohol. A disadvantage of this compound is its relatively short half-life. The individual must take it twice a day, with the result that the person could discontinue its use a day or so before drinking, with minimal to no drug-induced blockage of the 5-HT₃ receptor. At this point, ondansetron remains an experimental compound.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

Given the theory behind the use of ondansetron as a 5-HT₃ blocker, one would assume that the SSRIs would also be useful in the treatment of the AUDs. Unfortunately, these compounds have been shown to be ineffective in the treatment of the alcohol use disorders, unless the patient should have a concurrent depressive disorder (Bohn, 2001; Mariani & Levin, 2004).

VARENICLINE

There is preliminary evidence based on research studies in which this compound (sold under the brand name of Chantix® for smoking cessation) was found to also be useful as an aid to alcohol use cessation. McKee and colleagues (2009) found that individuals who drank heavily and who also smoked were less likely to smoke when given varenicline than were those who received a placebo. They also reported having fewer periods of craving for alcohol. The authors found that 80% of their research sample did not drink during the study period, as compared with only 30% of those who received a placebo, suggesting that there is need for further study into varenicline as a possible aid to alcohol use cessation.

PRazosin

There is some evidence supporting the use of prazosin, an alpha-1 adrenergic antagonist, might be useful in the

treatment of alcohol dependence (Simpson et al., 2008). This compound is normally used to treat hypertension and is sold under a variety of brand names. A research study involving only 24 subjects did find that those persons who received this medication reported drinking fewer days of the week as compared to the control group, although there was no difference between the two groups as to the amount of alcohol consumed per session (Simpson et al., 2008).

ANTIHYPERTENSIVE AGENTS

Adjunctive treatment for the alcohol withdrawal syndrome often involves the use of medications more traditionally used as antihypertensives. Clonidine, one such compound, limits autonomic nervous system hyperactivity, which is often seen in the AWS. The various β -blocker compounds also limit central nervous system over-stimulation, and are thought to reduce the period of time required for benzodiazepine support during the AWS (Greenberg, 2010).

PHENOBARBITAL

This medication is an alternative to the benzodiazepines, and like the benzodiazepines it has the additional advantage of reducing the possibility of withdrawal seizures during the AWS (Greenberg, 2010).

Section Summary

Although the search for pharmacological agents that might assist a person with an AUD to abstain from future alcohol use is limited, there is evidence that some current and experimental compounds might assist the individual in this task. Major pharmaceutical companies, however, are not committed to the search for such compounds, and if such a medication were to be found it probably will be as an incidental finding for a pharmaceutical introduced for another disease state. Further, there is a danger of "mission creep" (Aldhous, 2010, p. 43), which is to say that if a new medication were to be found effective in the treatment of the AUDs, then physicians might be tempted to say to a patient, "You show signs of *possibly* having an AUD, so let's put you on this medication as a precaution." Another form of mission creep is when the diagnostic criteria become less strict (which is a risk with the current diagnostic criteria for AUDs, given only two out of 11 criteria are needed), allowing the number of potential patients who could legitimately be prescribed a new medication to increase.¹⁴ Finally, there are

¹⁴An excellent example of this process might be seen in the marketing and prescribing tactics used by pharmaceutical companies that produce medications prescribed for erectile dysfunction. Over the past 20 years or so, the suggested use of these medications went from men with pathological erectile dysfunction to all men who experience erectile dysfunction, even if it is a normal part of aging. In receiving such a medication, those individuals with milder forms of this problem are also exposed to the dangers inherent in any medication use.

¹³Formerly known as *manic-depression*.

no diagnostic criteria that can be used to identify those individuals who might best benefit from pharmacotherapy for an alcohol use disorder (Aldhous, 2010).

Pharmacological Treatment of Stimulant Use Disorders

At this point, there are no known reliable pharmacological treatments for the stimulant use disorders (Haney, 2008; McLellan, 2008; Jayaram-Lindstrom, Hammarberg, Beck, & Franck, 2008; Sherman et al., 2017), although there is preliminary evidence for use of an analog of Modafinil® for use with cocaine misuse (Zhang et al., 2017). Scientists are exploring a number of lines of research in an attempt to identify such a compound(s) (Ling, Rawson, & Shoptaw, 2006; Winslow, Vorhees, & Pehl, 2007; Zhang et al., 2017). Although the amphetamines and cocaine are both classified as CNS stimulants, it should be pointed out that medications under investigation for possible use in treating other stimulant use disorders might not work for persons with cocaine use disorders, nor would the reverse automatically be true (Haney, 2008).

Bupropion

Initial clinical trials have indicated that this compound might help to block the craving that many individuals who use amphetamines, especially methamphetamine, experience in the early stages of recovery. Further research to confirm these initial research studies is ongoing at this time (Rawson & Ling, 2008).

Mirtazapine

Colfax and colleagues (2011) explored the use of mirtazapine as a possible adjunct to the treatment of methamphetamine addiction. The authors found a modest reduction in methamphetamine use levels in spite of poor medication adherence, suggesting a need for further research into the possible application of this compound to the treatment of methamphetamine addiction.

Modafinil

This is a compound sold to treat narcolepsy; it appears to hold some promise in the treatment of methamphetamine use disorders through its ability to activate some of the nerve pathways involved in attentiveness, without initiating the reward cascade (Rawson & Ling, 2008; Vocci & Elkashef,

2009). Further research into the utility of this compound in the treatment of the amphetamine use disorders is needed (Vocci & Elkashef, 2009).

Naltrexone

There is preliminary evidence suggesting that naltrexone can reduce the incentive to misuse amphetamines (Jayaram-Lindstrom et al., 2008). The causal mechanism for this effect is not clear; however, since naltrexone blocks the endogenous opiate receptors involved in the pleasure cascade, this might block the ability of the amphetamines to induce euphoria and thus the incentive for their use. The authors found that 62% of their research sample who were placed on naltrexone remained compliant with taking the medication, and that at week 12 of the study these participants reported less subjective craving for amphetamines than did those who were not on naltrexone. Research into the possible utility of this compound in the pharmacological treatment of amphetamine addiction continues at this time (Vocci & Elkashef, 2009).

Topiramate

As an anticonvulsant, this compound appears to normalize neural activity at seizure focal points in the brain, although it has multiple binding sites throughout the brain. The anticonvulsant properties of topiramate suggest that it might also help to normalize neural functioning during the period of acute withdrawal from methamphetamine. Research into this possibility is in progress at this time (Rawson & Ling, 2008; Vocci & Elkashef, 2009).

Gamma-Vinyl-GABA (Vigabatrin®)

This is an anticonvulsant medication approved for use in Europe, but not in the United States. It functions as a dopamine receptor antagonist in the nucleus accumbens, which is involved in the reward cascade. It is under investigation as a possible pharmacological treatment for the amphetamine use disorders at this time (Vocci & Elkashef, 2009).

Immunological Therapies

There are a number of programs under way attempting to use the immune system to “attack” amphetamine (especially methamphetamine) molecules in the circulation. This would prevent the amphetamine molecule from binding at the receptor site, thus preventing it from inducing any sense of pleasure (Knaresboro, 2011; Vocci & Elkashef, 2009).

Pharmacological Interventions for Cocaine Use Disorders

At least 19 compounds have been considered as possible pharmaceutical interventions for cocaine use disorders, without a single compound being found to be effective in this role (Lehne, 2013; Payer & London, 2009; Sherman et al., 2017). It is also important to point out that although both the amphetamines and cocaine are classified as CNS stimulants, there is little reason to suspect that a compound found to be useful in treating the other stimulant use disorders would automatically be effective in treating cocaine use disorders (Haney, 2008).

At one point, researchers thought that the antidepressant medications might help control post-cocaine craving, but research did not support this expectation (Kosten & O'Connor, 2003).

Another medication that is being examined as a possible pharmacological support for the treatment of the cocaine use disorders is *baclofen*, a muscle relaxant that is apparently able to reduce the individual's emotional responsiveness to conditioned cocaine use cues (Kampman, 2005). Finally, the anticonvulsant topiramate also appears to have a modest effect in helping to prevent a relapse back to active cocaine use following detoxification (Kampman, 2005).

Experimental Pharmacological Interventions for the Cocaine Use Disorders

In an interesting approach to the treatment of cocaine use disorders, researchers have explored the use of the antipsychotic medication aripiprazole to block cocaine craving in rats, and found that the experimental animals were less likely to resume self-administration of cocaine if they received aripiprazole (Feltstein, Altar, & See, 2007). This effect was dose-dependent, with those rats receiving the highest doses having the lowest rates of apparent cocaine-seeking behaviors. Since aripiprazole blocks the dopamine receptor sites in the brain, and cocaine affects these same receptor sites, the observed effects do make clinical sense. However, further research is needed to determine whether this medication would be effective in treating human subjects with the same results as those observed in the original experiment.

BUPRENORPHINE

The initial research studies suggested that this compound might be useful in the treatment of cocaine misuse or dependence. However, subsequent research has failed to consistently replicate the original studies, suggesting that this

medication probably is not effective in the treatment of cocaine use disorders (Kosten, Sofuoglu, & Gardner, 2008). Research into the possible utility of this medication in the pharmacological treatment for cocaine is ongoing.

CLONIDINE

Early experimental studies have suggested that this antihypertensive might be useful in curbing cocaine craving (Kosten et al., 2008).

DESIPRAMINE

There is mixed evidence that this antidepressant compound might reduce cocaine craving, but it is useful in those who use cocaine and who are also depressed.

DISULFIRAM

The use of disulfiram in the treatment of cocaine use disorders has received mixed results. Evidence suggesting that disulfiram¹⁵ might reduce cocaine post-withdrawal craving by increasing norepinephrine levels in the brain has been suggested (Sofuoglu & Kosten, 2004). This compound also functions as an indirect dopamine agonist by inhibiting the action of the enzyme dopamine beta hydroxylase. In theory, when a patient on disulfiram uses cocaine, she or he will experience an intense feeling of dysphoria (Kampman, 2005; Rounsaville, 2006). However, the team of Oliveto and colleagues (2010) failed to find evidence of a positive effect in patients recovering from opiate use disorders who were using cocaine and were stabilized on methadone. The authors called for further research into the possible use of disulfiram in the treatment of cocaine use disorders.

GABITRIL®

There is also evidence that a medication used as an adjunct to control seizures known by the name of tiagabine (sold under the brand name Gabitril®) might be of use in treating cocaine craving during the early stages of recovery. This compound functions as a GABA reuptake blocker, thus enhancing the sedating effects of GABA¹⁶ during the early stages of recovery (Heidbreder & Hagan, 2005).

IMMUNOLOGICAL METHODS

Researchers are also attempting to teach the body's immune system to attack cocaine molecules (Sergio, 2008; Knaraboro, 2011). This is done by attaching a foreign molecule, such as a biological toxin known to trigger a strong immune system response, to the cocaine molecules. Over time, the immune system "learns" to attack the cocaine molecules before they reach the brain induce any euphoria for the individual who uses cocaine (Sergio, 2008). This approach appears to have

¹⁵Discussed earlier in this chapter.

¹⁶Or counteracting the activating effects of NMDA, depending on how you want to look at it.

promise, although the initial vaccine was found to be only 38% effective in stimulating the addict's body into producing sufficient numbers of antibodies to suppress cocaine's effects, and these effects only lasted for about 2 months, thus making revaccination necessary every 2 months (Martell et al., 2009). However, the development of such a vaccine raises profound ethical questions: Does society have the right to force a cocaine-dependent individual to accept the vaccine, for example (Horstman, 2010)? If it is discovered after the vaccine has been in use for a period of time that it can induce debilitating side effects, does the individual forced to take the vaccine have right to legal redress against the state? Further research into this treatment approach is ongoing (Knaresboro, 2011), and the ethical implications of this vaccine must be addressed.

METHADONE

Animal research suggests the possibility that methadone (discussed below) might prove of value in the treatment of cocaine use disorders (Leri et al., 2008). The authors of this study concluded that steady-state methadone elevated the mu opioid receptor **mRNA**¹⁷ expression in the nucleus accumbens and basolateral amygdala regions of the rat brain, reducing the reinforcing effects of cocaine for the experimental animals. However, the applicability of this research to humans remains unproven. While these medications appear promising, to date no single medication, or combination of medications, has emerged to provide pharmacological support during the early stages of recovery from cocaine addiction.

MODAFINIL

This compound, which is normally used to control the symptoms of attention deficit hyperactivity disorder (ADHD), has been found in an initial study to normalize sleep patterns in newly abstinent cocaine addicts experiencing sleep problems (Morgan, Pace-Schott, Pittman, Stickgold, & Malison, 2010). The authors found that the administration of a therapeutic dose of modafinil to a small research sample in the morning resulted in increased daytime sleep latency and reduction in the level of subjective daytime sleepiness, while improving nighttime sleep. As noted earlier, recent research of a Modafinil analog shows promise for use with cocaine misuse (Zhang et al., 2017). Further research into the effects on cocaine withdrawal and stabilization of sleep patterns in the acute phase of cocaine withdrawal are needed.

PROPRANOLOL

There is preliminary evidence that the β -blocker (beta-blocker) propranolol might also prove useful during acute cocaine withdrawal (Kampman, 2005). This is accomplished by

a β -blocker–induced reduction in the individual's sensitivity to both adrenalin and noradrenalin, thus reducing his or her feelings of anxiety and agitation during this period (Kampman, 2005). Further research into the possible use of this compound in the treatment of the cocaine use disorders is needed.

TIAGABINE

This compound is a GABA reuptake inhibitor, and has been found to reduce the frequency of cocaine use and the amount of cocaine use in research subjects over a 10-week period of time (Kosten et al., 2008).

TOPIRAMATE

Originally introduced as an anticonvulsant, this compound appears to reduce the desire to use cocaine, but the original studies must be replicated to ensure that it is indeed effective when used to treat cocaine use disorders (Kosten et al., 2008).

STIMULANT REPLACEMENT THERAPIES

Methylphenidate, a medication approved for treatment of ADHD, has been investigated as a stimulant replacement, with some mixed results to date (Sherman et al., 2017). Additionally, use of Adderall® to help those who have a CUD and ADHD has gained some research support (Levin et al., 2015).

Pharmacological Treatment of Inhalant Use Disorders

There are no known pharmacological treatments specifically for the inhalant use disorders (Brust, 2004). Depending on the comorbid conditions, as well as inhalant-induced medical complications, a wide range of compounds might be employed to assist the individual in recovering from the misuse of these compounds.

Pharmacological Treatment of Marijuana Use Disorders

At this time, there are no medications that specifically treat marijuana use disorders (Danovitch & Gorelick, 2012; Sheff, Warren, Ketcham, & Evan, 2007). An interesting study conducted by Levin, McDowell, Evans, Nunes, et. al. (2004) explored the possibility that the anticonvulsant medication divalproex sodium could be used to treat marijuana misuse. The subjects in this study reported lower levels of marijuana craving while taking divalproex sodium, but there was little evidence of sustained abstinence from marijuana use in this research sample. The compounds buspirone and rimonabant have demonstrated some promise in controlling marijuana craving, although it would appear that cognitive-behavioral psychotherapy and/or behavioral psychotherapy offer greater

¹⁷See Glossary.

promise in marijuana dependence (Benyamina, Lecacheux, Blecha, Reynaud, & Lukasiewicz, 2008).

Pharmacological Treatment of Opioid Use Disorders

There are four subcategories of medications used in the treatment of opioid use disorders (OUDs): (1) medications to treat opioid overdoses, (2) medications used to control the symptoms of the opioid withdrawal syndrome, (3) opioid agonist agents to block opioid withdrawal symptoms, and (4) medications for relapse prevention. Each of these subgroups of compounds will be discussed in turn.

Medications to Treat Opioid Overdose

The mainstay treatment is Narcan (naloxone hydrochloride), with appropriate medical support (respiratory support, etc.). This compound is a pure opioid antagonist, and is currently administered by nasal spray or injection (Sherman et al., 2017). When injected, it reverses the sedation, respiratory depression, and hypotension induced by an opioid overdose, with the effects usually beginning within 2 minutes. Unfortunately, it has a relatively short half-life (estimated at approximately 30–80 minutes), and so multiple doses might be necessary before the patient has completely recovered from the overdose. A second side effect of Narcan is that it will induce the opioid withdrawal syndrome at the same time that it is reversing the opioid overdose.

The pharmacokinetics of Narcan are quite well studied. It is metabolized in the liver, and 25–40% of the original dose is excreted in the urine within 6 hours (Thompson, 2011). There is limited protein binding noted, and this compound will cross the placenta into the fetal circulation.¹⁸ It is not known at the present time whether this compound will cross over into breast milk.

Compounds to Treat Opioid Withdrawal

The opioid withdrawal syndrome can cause some degree of physical distress to the patient being withdrawn from narcotic analgesics. This is true for the patient who has been receiving narcotic analgesics after an extended period of medical treatment, and to the person who is physically dependent on any of the legal or illegal opioids available for misuse. In

this section, we will examine the medications most commonly utilized to help control the symptoms of the opioid withdrawal syndrome.

The opioid withdrawal syndrome does not automatically mean that the patient is misusing opioids. Patients who have suffered a severe injury that requires extended hospitalization, or repeated hospitalizations, and who are prescribed narcotic analgesics will often develop an **iatrogenic**¹⁹ addiction, although many physicians find it less threatening to the patient to refer to their condition as a reflection of the process of a degree of **neuroadaptation**²⁰ to the prescribed medication(s). To minimize the patient's withdrawal distress, physicians will often set up a gradual "taper" program to allow the individual's body to gradually adapt to lower doses of narcotic analgesics, minimizing the physical distress, the goal being that the patient will eventually discontinue the use of narcotic analgesics.

METHADONE

Methadone is often used by physicians for the taper process described in the last paragraph. The extended half-life of methadone makes it ideal for opioid withdrawal programs. This compound also has a significant misuse potential, and it can be quite dangerous if misused (Breggin, 2008). While some physicians and many members of the general public believe that methadone withdrawal for the individual struggling with an OUD is a waste of time, this stance appears to reflect preconceived prejudice rather than scientific data. It is simply impossible to determine who will remain abstinent from opioids even for just 4 weeks following detoxification, a fact that appears to justify methadone as an aid to opioid withdrawal for all persons who wish this therapy adjunct (Dijkstra, De Jong, Krabbe, & van der Staak, 2008). Further, various forms of pharmacological support during the opioid withdrawal process increase the chance that the patient will remain in abstinence-centered rehabilitation programs longer following the completion of the withdrawal process (Dijkstra et al., 2008).

While it is possible to carry out a methadone taper on an outpatient basis, most programs do so on an inpatient basis. The successful completion rate for an outpatient opioid detoxification regimen is only 17%, as opposed to 80% of those who are detoxified on an inpatient basis (Polydorou & Kleber, 2008). Also, there is a danger that the patient has also been using other compounds besides narcotic analgesics, or that the individual will attempt to intermix different chemicals, either to avoid withdrawal discomfort or to

¹⁸This is a matter of some concern, since it means that the fetus will also immediately go into opioid withdrawal if the mother is an opioid addict, even if the fetus is in utero.

¹⁹See Glossary.

²⁰See Glossary.

find an alternative combination of drugs to bring about a desired state of euphoria. Such person-directed polypharmacy brings with it the danger of an inadvertent overdose and possible death. Use of multiple substances reduces the patient's potential for successfully completing the withdrawal sequence and of accepting a referral to a rehabilitation program. Inpatient detoxification programs also avoid the danger of medication diversion, since the patient receives the prescribed dose of methadone as administered by staff. Finally, inpatient detoxification allows for medical supervision of the patients in case of unreported concurrent medical problems.

Initially, the patient is observed until the onset of withdrawal symptoms. Then oral doses of methadone are administered in increments of 10 mg/hour until the withdrawal symptoms are brought under control (Collins & Kleber, 2004; Polydorou & Kleber, 2008). This then becomes the starting dose for the withdrawal sequence on day two, when the patient receives this same dose all at once. Perhaps, in a hypothetical case, a patient required eight 10-mg doses before his or her withdrawal symptoms are initially brought under control. On day two this patient would receive a single 80-mg dose, usually in the morning. Then the patient's daily dose of methadone is reduced by 5–10 mg/day until she or he is completely withdrawn from all narcotics (Collins & Kleber, 2004). Sometimes the physician will order a slower taper when the daily dose reaches 10 mg/day, perhaps reducing the individual's daily methadone dose by only 2 mg/day, a process that remains unproven in terms of patient retention (Collins & Kleber, 2004).

Patients must be reminded that when their daily methadone reaches 30 mg (or in some cases less), they will experience some degree of withdrawal distress. There is no symptom-free withdrawal, and it is at this point that patient retention becomes a problem. Extended withdrawal regimens, some lasting up to 180 days, have been used in the hopes of improving patient retention. This approach does not appear to be more effective than the traditional 5–21-day methadone withdrawal cycle (O'Connor, 2000). An interesting approach is the slow reduction of the patient's daily methadone requirements until the individual reaches a 30 mg/day dosage level. At this point the patient is switched to buprenorphine (discussed below), and then tapered from buprenorphine over the appropriate period of time (Polydorou & Kleber, 2008). There is a need for further research into the efficacy of this approach.

BUPRENORPHINE

This compound, used in some opioid agonist programs, has also become a popular agent for control of the withdrawal symptoms from narcotics. When used in this capacity, the

patient is observed until they demonstrate a moderate level of withdrawal symptoms, a process that usually requires 8–12 hours. At that point, 2–4 mg of buprenorphine is administered in a sublingual dose (Polydorou & Kleber, 2008). If the withdrawal symptoms continue for another hour, another 2–4 mg of buprenorphine is administered in a sublingual dose. Yet a third sublingual dose of 2–4 mg of buprenorphine might be necessary to control the individual's withdrawal symptoms in extreme cases. Once the withdrawal symptoms are controlled, the individual's daily dose of buprenorphine is slowly reduced (usually at a rate of 1–2 mg/day) until the taper is completed. It should be noted, however, that elderly patients are likely to experience periods of respiratory depression when taking buprenorphine, and thus this medication should be used with caution in this age group to avoid exacerbation of respiratory problems (Klimstra & Mahgoub, 2010). It should be noted, however, that persons taking buprenorphine and are taking the antibiotic Rifampin® for a tuberculosis infection will experience opioid withdrawal symptoms because of the ability of Rifampin to induce liver enzymes that speed the buprenorphine biotransformation process.

CLONIDINE

Clonidine was originally developed as an antihypertensive agent. It also has a mild analgesic effect, although it is rarely if ever used in this capacity (Polydorou & Kleber, 2008). As was discussed in Chapter 11, narcotic analgesics suppress the action of the locus ceruleus region of the brain. This region of the brain becomes hyper-reactive during narcotics withdrawal, contributing to the individual's distress. Clonidine, which is technically an alpha-2 adrenergic agonist, helps to suppress the activity of the locus ceruleus, reducing the individual's withdrawal discomfort and distress. However, it has been found that clonidine-assisted withdrawal by itself results in significantly higher patient dropout rates than does a withdrawal regimen in which clonidine is used in combination with other compounds (Weiss, Potter, & Iannucci, 2008). This would seem to reflect the fact that clonidine does not completely control the individual's craving for opioids.

Another disadvantage of clonidine-assisted withdrawal is that this compound is an antihypertensive, and can cause abnormally low blood pressure levels (increasing the risk of patient falls) in many persons. Also, many patients have learned to combine clonidine with methadone, alcohol, benzodiazepines, or other compounds to induce a feeling of euphoria. Thus, health care professionals must closely monitor the patient to ensure patient safety and minimize the danger of non-prescribed drug use during the withdrawal process.

Experimental Methods of Opiate Withdrawal

ULTRA-RAPID OPIATE WITHDRAWAL

In the late 1990s, the concept of “ultra-rapid” opiate withdrawal was introduced. Developed at the Center for Investigation and Treatment of Addiction (CITA) in Israel, the process of ultra-rapid detoxification from opiates is carried out when the patient is in a chemically induced coma to minimize or totally avoid opiate withdrawal–related discomfort (Kaye et al., 2003; Whitten, 2006). After the coma is induced, the patient receives both clonidine and opiate antagonists, and the entire withdrawal process is completed within a single day. While there was a great deal of media attention when this procedure was first introduced, follow-up studies have revealed that it is only about as effective as traditional methods of opioid detoxification (Collins, Kleber, Whittington, & Heitler, 2005; Polydorou & Kleber, 2008; Whitten, 2006). There is little evidence to suggest that patients who go through this process are more likely to abstain from further opioid use than those who are detoxified through traditional methods, raising questions as to the need for such a costly treatment procedure that carries with it the risk of serious, potentially lethal, outcomes (Brust, 2004; Collins & Kleber, 2004; Kosten & O'Connor, 2003; Whitten, 2006).

Opiate Agonist Agents to Treat Opioid Use Disorders

The use of opioid agonist agents is based on the theory that, by blocking some of the opioid receptor sites, it will be possible to control, if not avoid, the patient's withdrawal symptoms without inducing euphoria. In this section, we will look at the commonly used opioid agonist agents used in opioid replacement therapies.

METHADONE

Perhaps the best known of the opiate agonist agents currently in use to treat opiate use disorder is methadone. Methadone is a synthetic narcotic analgesic developed just before World War II and extensively used by German physicians in that war in treating battlefield injuries. It is well absorbed following oral, intramuscular, and intravenous injections (Toombs & Kral, 2005). Currently, methadone is being used to treat persistent pain such as that encountered with certain ongoing medical disorders, as well as the control of opiate withdrawal symptoms, and in the context of methadone maintenance programs (MMPs). As its popularity as the medication of choice for various medical disorders has increased, so have the number of serious, if not lethal, drug overdoses involving methadone.

When used properly as an adjunct to the rehabilitation of persons addicted to opioids, methadone is relatively safe.²¹ The mortality associated with methadone maintenance programs is 1,500% lower than untreated opiate use disorder, a fact that supports its use in the control of opioid withdrawal symptoms for those who are addicted to narcotics (“Methadone overdose in MMT,” 2007). The vast majority of deaths associated with methadone use are caused by overdoses of methadone obtained from illicit sources. However, the danger of drug–drug interactions between prescribed methadone and other prescription medications can also result in a fatal reaction (“Methadone overdose in MMT,” 2007). Further, even therapeutic doses of methadone have the potential to cause cardiac arrhythmias, as discussed in the section on complications of prescribed methadone use, below.

HISTORY

The use of methadone to control the craving for narcotics that so often disrupts efforts at rehabilitation was first explored by Dole and Nyswander in the mid-1960s (Dole, 1988; Dole & Nyswander, 1965). There was a wave of heroin addiction in the United States at the time, and the standard treatment²² had proven inadequate to meet the need for rehabilitation at the time. Dole and Nyswander (1965) suggested that long-term opioid misuse caused permanent changes in the brain's structure on a cellular level, and that these changes contributed to the addict's experience of craving for opioids if they could not obtain their drugs. This craving was hypothesized to continue for months, or even years, after the individual's last use of a narcotic, prompting the individual to start to misuse opioids to feel “normal” again (Dole & Nyswander, 1965). The authors hypothesized that if a compound could be found that would block the individual's craving for opioids, it would then be possible for the individual to participate in a psychosocial rehabilitation program (Dole & Nyswander, 1965).

Dole and Nyswander found that subanalgesic doses of oral methadone would block the individual's craving for opioids for at least 24 hours (Kreek, 2000). However, in an excellent example of how one department of the federal government does not know what another department is doing, the Drug Enforcement Administration (DEA) threatened to arrest Dole and Nyswander (both federal employees working for another federal agency) for conducting this line of research (“After 40 years the basics of MMT are still valid,”

²¹ All medications carry a degree of risk, even when used as prescribed.

²² There were just two treatment centers for narcotics addicts in the 1960s, both controlled by the federal government. These programs essentially provided just detoxification services for opioid addicts, who in most cases returned to narcotics use shortly after their discharge from the treatment center.

2005). Eventually, the DEA relented, and Dole and Nyswander were allowed to continue their research.

PHARMACOKINETICS AND CLINICAL APPLICATION

It has been found that to prevent withdrawal symptoms from opioids, only 25–35% of the opioid receptor sites need to be occupied (Kreek, 2000; Schottenfeld, 2008). Further, the pharmacokinetics of methadone made it possible for once-daily administration for the control of opioid withdrawal symptoms. These factors made methadone “corrective but not curative” of opioid addiction (Dole, 1988, p. 3025). In spite of its potential in controlling withdrawal symptoms, methadone does not change the individual’s personality, vocational skills, or support system (Gerada, 2005). Following stabilization on methadone, the individual will still require psychosocial counseling (Dole, 1988), and it might require a number of years before significant social or vocational progress is seen (Schottenfeld, 2008).

As noted in the last paragraph, to be effective, the patient must receive a sufficient dose of methadone to block the craving for narcotics, which research has found requires a minimum dosage level of 80 mg/day (Dole & Nyswander, 1965). Unfortunately, at least one-third of existing programs prescribe no more than 60 mg/day for program participants (Pollack & D’Aunno, 2008),²³ in spite of the observation by Virani and colleagues (2009) that doses of 100 mg/day are usually sufficient to control the individual’s symptoms. This can cause the patient to experience subclinical withdrawal symptoms, contributing to the risk of relapse to active drug use. Further, consumption of four or more alcoholic drinks a day will reduce the blood methadone levels, as the alcohol increases the speed of methadone biotransformation (Borg, Kravets, & Kreek, 2009). Thus, the individual on methadone maintenance must abstain from alcohol to avoid inducing subclinical blood levels of methadone through concurrent alcohol use.

When utilized appropriately, methadone maintenance programs have been found to be cost-effective, with each dollar invested in such programs ultimately providing a return of \$38 through reduced health care costs, criminal activity, and increased employment (Clausen, Anchersen, & Waal, 2008; Zarkin, Dunlap, Hicks, & Mamo, 2005). In spite of these apparent advantages, methadone maintenance is still extremely controversial and subject to many misperceptions, such as that methadone maintenance simply replaces one addiction with another; there is also a shortage of physicians with the proper training to prescribe methadone for maintenance programs (Volkow, Frieden, Hyde, & Cha, 2014).

COMPLICATIONS OF PRESCRIBED METHADONE USE

If a patient on an MMP is injured and requires analgesia, MMP participants require *more* of a narcotic analgesic to achieve the same degree of pain relief as those who are not misusing opioids (Schottenfeld, 2008; Toombs & Kral, 2005). Methadone occupies less than 35% of mu opioid receptors to block the craving for narcotics, a level far too low to achieve significant levels of analgesia (Schottenfeld, 2008). Unfortunately, many physicians continue to dismiss the need for additional analgesic medications because the patient “is on methadone, and should not need any additional medications” following surgery or injury, causing many patients on MMPs to suffer needless, often extreme pain following an accident or injury.

A second, overlapping concern is the potential for multiple health care providers to be working with the same individual (Walley, Farrar, Cheng, Alford, & Samet, 2009). Research has found that the primary health care provider is unaware of the patient’s participation in a methadone maintenance program in 30% of cases. Because of this fragmentation of care, 69% of patients on a methadone maintenance program were receiving concurrent prescriptions for at least one medication that could interact with the methadone with potentially fatal results (Walley et al., 2009). Another important patient safety consideration is that methadone has the potential to induce or exacerbate potentially fatal cardiac arrhythmias including **torsade de pointes** (Justo, Gal-Oz, Paran, & Seltser, 2006; Roden, 2004; Tatro, 2009).²⁴ Periodic reassessment of the patient’s cardiac risk status, including serial electrocardiogram (EKG) studies, should be carried out by the prescribing physician (Schottenfeld, 2008).

Another, often unanticipated problem with methadone maintenance programs is the potential for insurance liability when a patient on methadone is involved in a motor vehicle accident or other incident in which another person is injured (“OTP liability and insurance claim trends,” 2010). Although there is little evidence that persons stabilized on methadone present a risk for impaired driving because of their methadone, the court system does not share this perspective, and the prescribing clinic assumes a financial liability should there be an accident (“OTP liability and insurance claim trends,” 2010). If the person is visibly impaired, this liability level is increased. Liability insurance and proper patient supervision, as well as updated information about concurrent medication use by a person on a methadone maintenance program, are essential to limit potential liability.

²³Often this is because the legislature in the state where the program is located prohibits the use of doses above 60 mg/day.

²⁴Discussed in Chapter 14.

APPLICATION OF METHADONE IN MAINTENANCE PROGRAMS

Following stabilization on methadone, the patient's medication is usually administered once a day, although some of the more progressive programs allow for "split dosing" to allow the patient to take part of the dose of methadone over a span of time. This medication is usually administered in liquid form to minimize the risk of drug diversion and is often mixed with fruit juice to make it easier to swallow. Patients who meet the federal and program guidelines may be permitted "take-home" dosing privileges, receiving a designated number of doses to be taken at home as per their medication schedule.

It is recommended that the patient remain involved with the MMP for a minimum period of 1 year to allow the individual sufficient time to address problems in living, and for some patients the commitment to methadone is a lifelong one, again reflecting that their addiction can be arrested, but not cured. Although psychosocial support services have been found to be useful adjuncts to the individual's rehabilitation, they are rarely offered. Kraft, Rothbard, Hadley, McLellan, and Asch (1997) concluded that three counseling sessions a week for each client was the most cost-effective in helping clients abstain from heroin use. Such counseling is labor-intensive, and unfortunately most programs have become little more than drug distribution centers some providing subtherapeutic doses of methadone while making no effort to provide actual rehabilitation services (Kauffman, 2003a, 2003b).

CRITICISM OF METHADONE MAINTENANCE PROGRAMS

Dole developed the model of methadone maintenance on the theory that opioid agonist treatment was similar to the role that insulin played in the control of diabetes (Kleber, 2002). This analogy, while useful in understanding the role that methadone might play in the pharmacological treatment of opioid dependence, is not automatically true. It is just a conceptual model, and it does not make opioid dependence a true disease state just because the analogy is useful (Marlowe & DeMatteo, 2003).

Critics of the methadone maintenance program model also suggest that it is simply switching their addiction from the drug(s) obtained from illicit sources to an addiction on a drug obtained from a legal source (Joseph, 2004; Kauffman, 2003a, 2003b; Kleber, 2002). Many patients in MMPs also misuse alcohol or cocaine, both compounds that speed the biotransformation of the methadone. In many cases they then claim a need for a higher dose of methadone than was originally prescribed to avoid withdrawal symptoms (Mendelson & Mello, 2008). Other participants in MMPs use these compounds while on methadone because they find that they enjoy the mixture of these chemicals. Further, many

patients on methadone maintenance programs attempt to obtain prescriptions (or illegal sources) for propoxyphene,²⁵ which enhances the effects of methadone and causes the user to experience a sense of euphoria. Other patients attempt to obtain benzodiazepines through either legal or illegal sources in an attempt to enhance the methadone-induced euphoria ("Dangers of benzodiazepine abuse during MMT," 2009). Both medications are ingested simultaneously for this reason, exposing the individual to the risk of benzodiazepine addiction and the potential for an overdose from the combined effects of the two medications.

At the very least, these observations suggest that MMPs are not the ultimate answer to the problem of opioid dependence. Dole acknowledged as much when he observed that methadone is "highly specific for the treatment of opiate addiction" (1989, p. 1880), doing little to block the euphoric effects of other forms of substance misuse. Further, it was acknowledged that medication diversion was a problem (Dole, 1995). There is anecdotal evidence that some opiate-dependent persons will purchase illicit methadone to carry out a methadone taper at home, reducing their drug dosage requirements. Finally, there is a significant dropout rate for patients in MMPs. These observations support the observation that MMPs are not the ultimate answer to the problem of opioid use disorders.

BUPRENORPHINE

This compound is a chemical cousin to morphine and has been playing an ever-growing role in the treatment of opiate use disorders. It is sold in the United States under the brand names of Suboxone® and Subutex®. When administered intravenously, it is thought to be 25–50 times as potent as morphine.²⁶ A standard conversion formula is that 0.3 mg of buprenorphine has the same analgesic potential as 10 mg of morphine (Fudala & O'Brien, 2005). It can be administered through intramuscular or intravenous injections, but is rapidly destroyed by gastric secretions, and so oral dosing is virtually impossible. It can, however, be administered sublingually. It is extensively biotransformed by the liver after being administered by this method, limiting its effectiveness as an analgesic. However, this characteristic, in combination with the ability to bind to the mu opioid receptor site for extended periods of time, makes it of value as an oral opioid agonist that can be used in much the same manner as methadone. It also makes it virtually impossible to overdose on buprenorphine (Collins & Leak, 2008).

²⁵The legal production of which, as noted in Chapter 11, has now been discontinued in the United States.

²⁶The side effects of buprenorphine are reviewed in Chapter 14.

The financial benefits of opiate agonist therapy with buprenorphine were illustrated in the conclusion of the team of Lynch and colleagues (2014), who found that the annual health care cost for a person in an integrated health care system who was on buprenorphine was approximately \$13,578, while the annual health care cost for a person dependent on opiates who was not on buprenorphine was approximately \$31,055. Thus, buprenorphine would appear to be cost-effective. Further, unlike methadone, buprenorphine does not appear to cause any delay in psychomotor or cognitive performance (Weiss, 2007).

Buprenorphine is highly lipid-bound (96%), providing a reservoir of medication that can control opioid withdrawal symptoms for an extended time (Weiss, 2007). When administered sublingually, it is absorbed by the blood-rich tissues that line the mouth. The bioavailability of buprenorphine is only 30–50% of that achieved after an intravenous dose (Donaher & Welsh, 2006). The medication that is absorbed then blocks the opioid receptor sites, acting much as methadone does in blocking the opioid withdrawal symptoms without inducing a significant degree of euphoria. Sublingual doses of 2–8 mg/day of buprenorphine are about as effective as 65 mg of methadone (Donaher & Welsh, 2006). There is some controversy about the maximum effective dose of buprenorphine when used as an opiate agonist. Donaher and Welsh (2006) suggested that doses up to 32 mg/day in divided doses might be necessary in extreme cases (Donaher & Welsh, 2006; Sofuoglu & Kosten, 2004). However, O'Brien (2011) recommended that if the individual has not been able to control his/her drug craving at doses of 16+ mg/day of buprenorphine, he or she should be switched to methadone agonist treatment.

The pharmacokinetics of buprenorphine are unique: The molecule first binds at the mu receptor site in the brain, preventing the development of craving for opiates. However, the molecule remains in the receptor site after binding to it, preventing other opiate molecules from gaining access to that receptor site. The result is that at high doses buprenorphine can induce the opiate withdrawal syndrome, and if administered to a person under the influence of another narcotic it can initiate the opiate withdrawal within seconds. Individuals dependent on narcotics must be drug free for several days before buprenorphine treatment is initiated to avoid forcing the individual to go through opiate withdrawal at the start of buprenorphine treatment (U.S. Department of Health and Human Services, 2004). At best, it is only as effective as methadone in controlling opioid withdrawal symptoms (Donaher & Welsh, 2006). There is a growing problem with drug diversion, as intravenously administered buprenorphine has some misuse potential (U.S. Department of Health and Human Services, 2004). For this

reason, buprenorphine is often mixed with naloxone, which will precipitate opiate withdrawal if the tablet is crushed and injected (Leinwand, 2000). Further, some centers advocate that buprenorphine only be administered in a supervised setting, so that the patient is not sent home with tablets that might later be diverted.

It has also been found to interact with a wide range of other compounds, including (but not limited to) benzodiazepines, alcohol, and other CNS depressants that might cause a potentially fatal drug potentiation effect. Buprenorphine has also been found to interact with many antiviral agents used to treat HIV infection (Fiellin, Rosenheck, & Kosten, 2001; Tatro, 2009). Also, its use in children or adolescents has not been approved by the Food and Drug Administration, which is a problem given the growing problem of adolescent opioid addiction (Fiellin, 2008).

An interesting experimental modification of buprenorphine was reported by Bai-Fang and colleagues (2004). The authors utilized an experimental polymer micro-encapsulated, long-acting form of buprenorphine injected into the user's body. This allowed for the gradual release of buprenorphine over 4–6 weeks, blocking narcotic-induced euphoria and allowing the patient to gradually discontinue the use of narcotics without significant distress, according to the authors. This method did demonstrate some promise, but has not been more fully developed as of this time.

Fiellin and colleagues (2014) warned that they found that opioid maintenance therapy was more effective than was a buprenorphine-based taper for persons who became dependent on narcotics as a result of prescription opioid misuse. The authors based this warning on their finding that patients who were placed on a buprenorphine taper were more likely to have evidence of illicit drug use when tested, and were less likely to remain abstinent from illicit narcotics than were those who were placed on an opioid agonist treatment program.

NALTREXONE

Originally, this compound was developed for the treatment of the alcohol use disorders, and as noted earlier in this chapter, it has also been found to be of limited value in the treatment of opioid use disorders. Naltrexone is an opioid antagonist blocking the mu opioid receptor site. Oral doses of naltrexone are well absorbed, and peak blood levels are achieved in about an hour. The half-life of naltrexone has been estimated to be between 3.9 and 10.3 hours, and clinical research suggests that naltrexone blocks the euphoric effects of misused opiates for up to 72 hours after it is last ingested. When used as an adjunct to the treatment of the opioid use disorders, 100 mg of the medication is usually administered every other day, with the patient receiving 150 mg on Friday to block opioid craving over the weekend.

The theory behind the use of naltrexone is that blocking the euphoric effects of the opioids would leave the individual with little incentive to misuse this class of medications. It does, however, present the danger of inducing the opioid withdrawal if administered before the patient has completely detoxified from the opioids. Ling, Mooney, and Wu (2012) recommended that the individual be opiate-free for several days before being started on naltrexone. Unfortunately, some individuals misusing opioids try to “shoot through” naltrexone by using exceptionally large doses of opiates, placing themselves at risk for a potentially fatal overdose (Ling et al., 2012).

While in theory naltrexone would seem to be useful in the treatment of opiate use disorders, it is not a “magic bullet” for the opioid use disorders (Kraly, 2009; Ling et al., 2012). Indeed, there is no *unequivocal* benefit from the use of this compound in the treatment of opiate use disorders (Kraly, 2009). It appears to be most effective for those patients who are motivated to follow treatment recommendations. Medication compliance is a problem: The vast majority of patients started on naltrexone discontinue the use of this medication within 6 months. One reason offered by those who use opiates for discontinuing the medication is that it does not make them feel “high” (Ling et al., 2012). Further, there is no suppression of opiate craving while the patient is on naltrexone, which often comes as a nasty surprise to the individual on this medication, and this is another reason many individuals choose not to use this medication.

In 2006, a time-release, injected form of naltrexone was introduced under the brand name of Vivitrol (*Prescribing Information*, 2006). The applicability of this preparation in the treatment of opioid use disorders has not been determined. However, its high price would prohibit its widespread use in the treatment of opioid use disorders even if it is found to be effective in the treatment of opioid use disorders. The danger of an individual switching from opioids to other drugs cannot be ignored. Ngo, Tait, and Hulse (2008) found that patients who had received naltrexone implants were more likely to require hospitalization for treatment of non-opioid overdoses in the first 6 months of the study, and after a 3-year follow-up period it was found that those patients in the naltrexone-implant sample were more likely to require hospitalization for (or die from) non-opiate overdoses. The authors called for further research into their observed findings to attempt to replicate these results. Thus, the applicability of naltrexone to the long-term treatment of opioid use disorders at best remains in doubt.

LAAM

Initial research suggested that LAAM²⁷ was useful as an opiate agonist agent that would function much like methadone

maintenance. The extended half-life of LAAM (>48 hours, as compared with methadone’s approximate 24-hour half-life) added the advantage that the patient would only need to come in for dosing every second or third day rather than daily, as in methadone maintenance programs. Unfortunately, shortly after it was introduced it was discovered that LAAM could induce potentially fatal cardiac arrhythmias at therapeutic doses, and the production of this product in the United States was discontinued in 2004 (Ivanov, Schulz, Palmero, & Newcorn, 2006).

EXPERIMENTAL COMPOUNDS FOR OPIATE USE DISORDERS

Ibogaine, an alkaloid obtained from the root bark of the shrub *Tabernathe iboga*, has been considered experimentally as a possible agent for the treatment for detoxification from opiates, stimulants, alcohol, and nicotine in particular. This shrub grows in certain regions of Africa, and has some hallucinogenic properties (Abrams, 2003). Either because or in spite of this characteristic, ibogaine is reputed to eliminate the individuals craving for opioids, especially in the earliest stages of recovery (Glick & Maisonneuve, 2000). Scientists are uncomfortable with the use of ibogaine itself, as evidence suggests that at high doses it can cause seizures and neural damage, and it can induce side-effects that are intolerable for many users.

However, researchers have also discovered that the major metabolite of ibogaine, a compound called noribogaine, might prove useful (Abrams, 2003). This compound has a half-life of several weeks, and a chemical structure that lends itself to manipulation by scientists who hope to find a way to retain its reputed benefits while avoiding the harsh side effects (Glick & Maisonneuve, 2000). An experimental compound known as 18-MC appears to accomplish this goal, but there are still many misconceptions and governmental bureaucratic hurdles that stand in the way of the clinical application of this compound, if it is found to be effective in human subjects.

Probuphine is a recently approved buprenorphine implant that was originally denied permission to be marketed by the Food and Drug Administration in 2013 for failing to demonstrate superior efficacy in treating opioid use disorders over existing treatments. In 2015, the manufacturer reapplied for a license to market this product for treatment of OUDs, citing new research studies that demonstrated its superiority over buprenorphine as an opioid antagonist.

IMMUNOLOGICAL THERAPIES

The first research into the possibility of using the body’s immune system to combat heroin use disorders was started in the 1970s, but the success of opioid agonist treatments such as methadone and buprenorphine put a halt to further

²⁷Or *L-alpha-acetylmethadol*.

research in this area (Knaresboro, 2011). However, researchers are now starting to again look at the possibility that the immune system could be recruited into the fight against the opiate use disorders, turning their attention first to the problem of heroin (Knaresboro, 2011).

Medications for Opioid Relapse Prevention

Although naltrexone has been approved by the FDA since the early 1980s for use with opioid use disorders, extended-release injectable naltrexone was not approved until 2010 (Sherman et al., 2017). This injection may be especially useful in those who are not successful with opioid replacement therapies, and it has showed some promising research results to date (Sherman et al., 2017).

Pharmacological Treatment of the Tobacco Use Disorders

Nicotine has been shown to be the most addictive of the vast number of compounds found in cigarette smoke, and thus has been the focus of a great deal of clinical research. Several pharmacological interventions for the tobacco use disorders center around nicotine replacement therapies. This both limits the individual's exposure to other chemicals and allows for a gradual reduction in nicotine dosage levels over an extended period. However, some research has raised questions about the long-term effectiveness of such techniques in smoking cessation (Alpert, Connolly, & Biener, 2011). The authors pointed out that statistically, individuals who used nicotine replacement aids as part of their smoking cessation program were just as likely to return to the use of tobacco as were those who did not use such pharmaceutical supports as part of their smoking cessation effort. We will briefly discuss some of the more common forms of pharmacological intervention for the tobacco use disorders.

Nicotine Replacement Systems

NICOTINE GUM

Nicotine-containing gum was first introduced as a prescription-only compound in 1984, but later became available without a prescription (Anczak & Nogler, 2003). It was hypothesized that this would provide a safe, convenient nicotine replacement mechanism for the smoker who wished to quit. The initial research suggested that 27% of patients who utilized nicotine-containing gum were smoke-free 6 months after the start of their abstinence program. However,

subsequent research has shown that the true abstinence rate for smokers who utilize nicotine-containing gum is no higher than that achieved by a placebo (Okuyemi, Nollen, & Ahluwalia, 2006).

Individuals who choose to quit smoking and who elect to use nicotine-containing gum either as the primary tool or as an adjunct to their smoking cessation program must learn a new way to chew gum in order to gain maximum effect. The individual must learn to chew the gum once or twice, and then “park” it between the gum and the cheek for a few moments before repeating the procedure. When this procedure is followed, 90% of the nicotine in that piece of gum is released within the first 30 minutes. However, a 2-mg piece of nicotine-containing gum will allow the user to achieve a blood nicotine level that is only about one-third of that achieved by smoking a cigarette. While the 4-mg preparation doubles this blood nicotine level, it still falls short of the amount of nicotine released into the blood by cigarette smoking. This may result in a craving for additional nicotine on the part of the smoker, who then discontinues the attempt to quit.

Further, nicotine-containing gum has been found to have many side effects, such as sore gums, excessive salivation, nausea, anorexia, headache, and the formation of ulcers on the gums where the person parked the gum. Beverages with a high acid content, such as orange juice or coffee,²⁸ also block the absorption of the nicotine from the gum. So the former-smoker-to-be must closely monitor the form of his or her beverage intake to avoid compounds that might negate the benefits of the gum. A recently identified danger in such nicotine-containing gum is that the nicotine in the gum might up-regulate the FOXM1 gene in the tissues that come into contact with the gum, increasing the individual's risk for the development of oral cancer (Gemenetzidis et al., 2009).

TRANSDERMAL NICOTINE PATCHES

These patches have been found to be moderately effective. Transdermal nicotine patches have been found to reduce the insomnia so often reported by individuals who attempt to quit smoking on their own, which is an advantage. It is generally assumed that only 3% of those who attempt to quit smoking on their own will be able to do so. The 10–16% success rate of smoking cessation for the first 6 months is thus a significant improvement, but this still means that 85% of individuals who attempt to quit fail to do so on this attempt at smoking cessation. This may reflect the fact that, in contrast to the nearly instantaneous delivery of nicotine to the circulation achieved with cigarette smoking, transdermal nicotine patches require

²⁸How many people smoke cigarettes but never drink coffee?

approximately an hour for blood nicotine levels to reach their peak. This time delay is hardly appropriate for a behavioral modification program designed to extinguish an undesired behavior. Finally, the blood nicotine levels achieved through the use of the transdermal nicotine patch often are lower than those achieved by the process of smoking, inducing a craving for additional nicotine.

However, there is a very real danger should the individual attempt to supplement their nicotine levels by smoking. Individuals who smoke, either while still wearing the nicotine patch or within an hour of removing the transdermal nicotine patch, are vulnerable to a nicotine toxicity that may potentially be fatal. It is recommended that if the individual should feel the need for additional nicotine, he or she should use nicotine-containing gum, or in extreme cases (as in an individual who has been smoking 3–4 packs a day), multiple skin patches might be used under the supervision of a physician. The transdermal nicotine patch can cause skin irritation, and so different sites around the body should be utilized on different days. Nicotine transdermal patch use has been associated with abnormal or disturbing dreams, insomnia, diarrhea, and a burning sensation where the patch is attached to the skin. Also, while it might seem obvious that the individuals would remove the last day's transdermal patch before attaching a new one, there have been cases where the patient has left the old skin patches in place.

The individual who has given up smoking is vulnerable to smoking cues in the first weeks and months following smoking cessation, and some patients become either psychologically or physically dependent on the transdermal nicotine patch. From a harm reduction viewpoint, this is an acceptable compromise since there are over 4,500 known compounds in cigarette smoke, and only one in the nicotine transdermal patch (Gitlow, 2007).

NICOTINE NASAL SPRAY

A nicotine-based nasal spray has recently been introduced, which is available only by prescription (Sofuoglu & Kosten, 2004). The user will administer one “puff” of the spray to each nostril, where the nicotine will be absorbed by the blood-rich tissues of the sinuses. The spray can be used up to 40 times a day. Within 10 minutes of administration, the blood nicotine level will reach two-thirds of the level seen when a smoker smokes one cigarette (Anczak & Nogler, 2003). Initially, it was suggested that the patient use this product for less than 6 months, in part because of a concern that he or she might become addicted to the nicotine spray. However, there has been little evidence that such addictions have developed (Anczak & Nogler, 2003). A degree of sinus irritation is possible from this spray, but there has been little research into whether this degree of sinus irritation is the same as that seen

when an individual smokes a cigarette. Individuals who used the nasal spray were less likely to gain weight during their cessation attempt, and tended to gain less weight than those who did not use the spray. Just under one-third of those who attempted to quit using this method remained smoke-free 6 months after quitting, as opposed to just 14% of those who received a placebo (Okuyemi et al., 2006).

In the late part of the 1990s, McNeil Pharmaceuticals introduced a nicotine “inhaler” for use by those smokers who were attempting to quit. The inhaler was housed in a device similar to that of a cigarette or cigar filter. This device was to be used in place of cigarettes, although it was held in the hand in a manner similar to the way that cigarettes are held. It will deliver 4 mg of nicotine to the user out of the 10 mg that is in the cartridge, and is designed for short-term use. Twenty-three percent of those who used the inhaler remained cigarette free for 6 months, as compared to just 11% of those who received a placebo (Okuyemi et al., 2006).

ELECTRONIC CIGARETTES AS AN AID TO SMOKING CESSATION

Electronic cigarettes (or e-cigarettes) were introduced in 2006 and are discussed in more detail in Chapter 15. It has been suggested that e-cigarettes will be of value in smoking cessation efforts, although to date individuals who use e-cigarettes for smoking cessation appear to have a success rate that is about the same as achieved through traditional pharmacologically supported smoking cessation (de Lange, 2014).

CYTISINE

Cytisine is an alkaloid compound obtained from the laburnum tree, which has been shown to be more effective than nicotine replacement therapies in assisting individuals to quit. It is prescribed for this reason in some European countries; however, the efficacy and safety studies carried out there did not meet U.S. standards, and so it is not prescribed in this country. When combined with short-term behavioral therapies, significantly more persons using cytisine were able to abstain from further tobacco use in the first 6 months of recovery than those using nicotine replacement therapies alone. However, cytisine users reported adverse symptoms such as nausea, vomiting, and various sleep disorders more often than persons who utilized a nicotine replacement therapy.

COMBINATION THERAPIES

An interesting approach was utilized by Piper and colleagues (2009), who used a combination of oral nicotine lozenges and transdermal nicotine patches to produce significantly higher abstinence rates than monotherapy approaches such as transdermal patches or bupropion alone. The study did

not utilize nicotine lozenges plus varenicline, which was a shortcoming of the study, but did suggest that the combination of transdermal nicotine patches and oral nicotine lozenges offered greater effectiveness to the smoker if they complied with medication dosing schedules. The authors found that medication compliance was an issue, with a positive correlation between compliance with dosing and smoking cessation.

Non-Nicotine Replacement Pharmaceuticals for Smoking Cessation

While it might be argued that nicotine replacement therapies reflect a form of “pharmaceutical” intervention for smoking cessation, in this section we will discuss non-replacement methods of smoking cessation intervention.

BUPROPION

This antidepressant’s primary effects are on the serotonin and dopamine neurotransmission systems. Often sold under the brand name of Wellbutrin® in the United States, it also has a mild acetylcholine reuptake blocking effect. This side effect of bupropion was found to control the craving for cigarettes in former smokers who were taking this antidepressant for the treatment of a depressive disorder. Further research demonstrated that 21–30% of those patients taking this medication as an aid to smoking cessation were able to remain smoke-free for 6 months, as opposed to only 10–19% of those receiving a placebo (Okuyemi et al., 2006). Bupropion was then marketed as an aid to smoking cessation under the brand name of Zyban®. However, questions have been raised concerning possible increased risk for aggression during the process of smoking cessation. Recent research reviews indicate that it is better than placebo for quitting after 6 months (Sherman et al., 2017).

CHANTIX® (VARENICLINE)²⁹

Varenicline was introduced as an aid to smoking cessation in 2006 (Alfonso, 2008). In the time since it was introduced, varenicline has been found to be the most effective pharmacological intervention for smoking cessation available. It is not perfect, and there is a need for research into other pharmacological agents that might assist smoking cessation (Ebbert, 2009). Varenicline functions as a partial agonist at selected nicotinic acetylcholine receptor sites,³⁰ partially stimulating these receptor sites without activating the dopamine cascade

necessary to cause pleasure, and blocking nicotine from these receptor sites when the individual smokes (*Chantix Prescribing Information*, 2006). Maximum blood levels are achieved 3–4 hours after a single dose, and steady-state blood levels are achieved after about 3–4 days of regular use at prescribed doses (*Chantix Prescribing Information*, 2006). Less than 20% of varenicline is protein-bound, and the elimination half-life of this compound is about 24 hours, with 92% of the drug being excreted in its original form (*Chantix Prescribing Information*, 2006).

The side-effect profile for varenicline includes (but is not limited to) nausea, abdominal pain, flatulence, visual problems, depression, suicidal thoughts or attempts, mood swings, vivid (sometimes frightening) dreams,³¹ rare reports of angina pectoris, myocardial infarction, a lower seizure threshold, and gingivitis (*Chantix Prescribing Information*, 2006; Rogers & Pies, 2008). The Food and Drug Administration requires a special warning for prescribers to the effect that varenicline use is a possible cause of increased aggression and possible suicidal thinking (Moore, Glenmullen, & Furberg, 2010; Price, 2009). These unprovoked thoughts or acts of violence disappeared when the medication was discontinued, and in three cases developed again when the medication was restarted (Moore et al., 2010). It should also be noted that persons with a preexisting history of depression who were placed on this medication tended to report feelings of tension or agitation, as well as irritability, anger, continued depression, confusion, and problems with concentration during the first 3 weeks of treatment (McClure et al., 2009).

Because patients with a preexisting psychiatric history were excluded from the original product safety and efficacy trials, the relationship between varenicline use and psychiatric symptoms remains unclear, according to authors McClure and colleagues (2009). The team of Moore, Furberg, Glenmullen, Maltsberger, and Singh (2011) went even further by examining the methodology used by the Food and Drug Administration and concluding that this *underestimated* the true risks associated with the use of this compound. The authors noted that the FDA limited its focus to persons taking varenicline who became hospitalized for depression or following a suicide attempt, a process that downplayed the true danger associated with this medication, because it did not include those cases of suicidal thinking or depression that did not result in hospitalization. Because of this, the authors recommended that it not be the first choice of clinicians for persons who want to stop smoking. This is consistent with the 2008 decision by the Federal Aviation

²⁹The generic name for this compound.

³⁰Technically the $\alpha 4\beta 2$ receptor site.

³¹Sometimes called “Chantix dreams.”

Administration that pilots and air traffic controllers not use this compound, in part because of its side-effect profile. Obviously, varenicline “is not a panacea for smoking cessation” (Klesges, Johnson, & Somes, 2006, p. 95). The benefits appear to last only about 12 weeks, possibly because of the process of neuroadaptation to the drug’s effects (Smith, 2008), and there is a need for further research into pharmacological therapies for smoking cessation.

While the above would suggest that varenicline is not a perfect pharmacological intervention for tobacco smoking, it is proving to be of value as an adjunct to the treatment of conditions such as the acute coronary syndrome (ACS) who also smoke. Eisenberg and colleagues (2015) found that nearly half of patients admitted for ACS were smoke-free 6 months after admission if varenicline was initiated while the patient was still hospitalized, as opposed to simply referring the patient to a stop-smoking clinic following discharge. Other evidence suggests that persons who are placed on this medication are significantly more likely to remain smoke-free at the end of 6 months compared with persons who were placed on bupropion or who received only a placebo (58% vs. 46% vs. 26%) (Cinciripini et al., 2013), suggesting that it is a valuable, if imperfect, aid to smoking cessation.

Experimental Compounds for Smoking Cessation

BUSPIRONE

It was once thought that buspirone might counteract the anxiety and agitation often experienced by smokers in the early stages of smoking cessation. However, subsequent research failed to support this theory, and it is not utilized as an aid to smoking cessation unless the smoker experiences high levels of anxiety during the smoking cessation process (Covey et al., 2000).

CLONIDINE

A number of clinicians have attempted to utilize the antihypertensive drug clonidine to control the craving for nicotine often reported in the early stages of smoking cessation. Although the initial studies were promising, subsequent research suggested that the side effects were so severe for the average user that it was not useful as an initial approach to smoking cessation (Anczak & Nogler, 2003). However, it might prove useful in the subpopulation of smokers who experience high levels of agitation when they attempt to quit smoking (Covey et al., 2000).

IMMUNOLOGICAL APPROACHES

Researchers have started to explore the potential for recruiting the body’s own immune system defenses against the nicotine molecule, with a number of experimental vaccines being

developed at this time (Arnold, 2015; Knaresboro, 2011). Although such vaccines are limited to laboratory studies involving animals, nicotine-, cocaine-, and amphetamine-specific vaccines are theoretically possible and potentially might be introduced in the next decade. These vaccines are designed to prime the body’s immune system to attack molecules of the target drug in the blood before they reach the brain, negating their potential to initiate the reward cascade.

INVERSINE (MECAMYLAMINE)

This is an antihypertensive compound that is an acetylcholine receptor antagonist, blocking the receptor sites in the brain. This compound would then block the individual’s craving for cigarettes, and it has been moderately successful in smoking cessation programs, although it has not found widespread use in this application.

NORTRIPTYLINE

This antidepressant is viewed as a second-line smoking cessation agent, in part because of its toxicity and potential for a fatal overdose if taken in excess. However, it might be useful in working with those attempting to quit smoking and who are also depressed, and there is a need for further research into the potential use of this compound in smoking cessation (George & Weinberger, 2008).

SILVER ACETATE

This is a compound used in Europe for many years as an aid to smoking cessation. It is available as a chewing gum and as a lozenge. When a person who has used silver acetate-containing chewing gum or lozenges smokes, they will experience a noxious, metallic taste, providing an immediate punishment that will help the smoker extinguish the desire to smoke. This compound is also quite dangerous. Massive doses can result in a *permanent* discoloration of the skin and body organs. Still, it is being examined as a possible aid to smoking cessation.

CLOZAPINE

Clozapine is an “atypical” antipsychotic medication that has been shown in a small number of studies to reduce the symptoms not only of psychosis, but also of substance misuse in dual-diagnosis patients (Lybrand & Caroff, 2009). The use of other atypical antipsychotic medications as aids in the treatment of SUD, especially in those patients with a comorbid psychotic disorder, has yielded mixed results, but does suggest that there is a need to determine whether these compounds offer any promise of assisting the individual (either with or without a psychotic condition) to abstain from smoking.

Chapter Summary

The pharmacological treatment of the substance use disorders, like the treatment of all other disease states, involves

the application of selected medications to either control the manifestations of the disease or cure it. Pharmaceutical companies often invest significant amounts of money to develop compounds for these purposes, but often dismiss the need to search for compounds to treat the substance use disorders, because the market is too limited to provide a reasonable financial return on their investment. Thus, most of the pharmacological compounds in use for the treatment of the SUDs are actually medications used to treat other conditions, which have been found to also be useful as pharmacological adjuncts to the treatment of substance use disorders.

Several subgroups of medications utilized as adjunctive treatments for SUDs were reviewed: (1) medications that control withdrawal symptoms, (2) medications that control the individual's craving for drugs, (3) aversive agents that cause dysphoria when certain compounds are used, (4) compounds used to treat concurrent psychiatric disorders, (5) agonist compounds used in certain "maintenance" programs, and (6) medications used to treat drug overdoses. Also, experimental methods by which the body's immune system might be trained to attack specific drug molecules for both cocaine, and possibly the amphetamines, were reviewed.



CHAPTER 34

Relapse and Other Problems Frequently Encountered in Substance Rehabilitation

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 34.1** Identify the commonly encountered problems in treating individuals with SUDs
- 34.2** Review the concerns related to treatment noncompliance
- 34.3** Define and describe concerns with lapse and relapse
- 34.4** Identify the most common causes of relapse
- 34.5** Consider the impact of pain on those struggling with SUDs
- 34.6** Review the concept of controlled drinking
- 34.7** Understand the use of toxicology testing in treating individuals with SUDs

Introduction

Although research has repeatedly demonstrated that treatment is more effective than criminal justice sanctions as a way of dealing with substance use disorders, treatment also is not a panacea. There are numerous problems that might arise for the client in either an inpatient or an outpatient substance rehabilitation program. In this chapter, we will look at some of the more common and potentially more serious problems encountered by rehabilitation professionals working with individuals misusing substances.

Common Problems

Limit Testing by Clients

One common misperception about substance professionals is that they are “bleeding hearts” who will excuse virtually any misdeed by clients because of their SUDs. However, some therapists in the early stages of their careers do attempt to “buy” client approval through such permissiveness. It is important to keep in mind the fact that caring for a client does *not* mean protecting him or

her from the natural consequences of his or her behavior! It is through these consequences that the client will come to see the need for change and learn the limits of healthy behavior.

Clients in therapeutic relationships, including those with SUDs, will often “test” therapeutic limits. This is done either consciously or unconsciously by the client in order to determine whether the therapist can be trusted, or, in some cases, if it is possible to find a way to control the therapist. Limit testing takes many different forms: The client might repeatedly miss appointments, or call to cancel a previously scheduled appointment at the last moment. Other clients might misuse alcohol or drugs while in a rehabilitation program. Such situations present the therapist with opportunities to demonstrate that dependability and consistency are part of the foundation of rehabilitation. For example, treatment programs that warn clients that a certain number of positive urine toxicology test results¹ will result in discharge from the program tend to have greater success than programs that fail to set such limits.

The Counselor and Treatment “Secrets”

One common method of manipulation often attempted by clients is when they request an individual conference with a staff member, and then confess to a rules infraction. Sometimes such confessions are made to a student or an intern at the rehabilitation facility. The client then begs the staff member to keep this a secret, for fear of being discharged from the program, put into jail by a probation officer who learns of this chemical use, divorce by an angry spouse, etc. The substance rehabilitation professional who honors this request then enters into a state of collusion with the client. This becomes a relationship in which the staff person, who is attempting to help the client outgrow addictive thinking, is instead enabling the client. Further, the client can then use the counselor’s silence as leverage for blackmail (“If you don’t do [fill in the blank], I’ll tell them that you didn’t report my relapse last week!” etc.). In correctional facilities, once a staff person brings contraband into the jail or prison, this also can be used as leverage for blackmail (“If you don’t bring in more contraband I will report you!”). The proper response to the problems mentioned above is for the staff person to properly document the initial discussion immediately, in writing and through proper channels. This can either be a memo to the facilities administration or an entry in the client’s progress notes. The staff person should also discuss the revelation with his or her immediate supervisor. This is all done without

malice, to ensure both uniform enforcement of the rules and accountability for the client, and to protect the staff person’s reputation.

A Double Standard

To illustrate the double standard as applied to the field of substance rehabilitation, consider the contrast between oncology treatment programs and substance treatment programs. Cancer programs do not insist that the person be “in remission” before being admitted for treatment. However, it is not uncommon for alcohol and drug rehabilitation programs to require abstinence before admission to treatment (Blume, 2005). Another example of this double standard is how a person with diabetes who is repeatedly admitted to the hospital for stabilization of their medical condition can be called a “brittle” diabetic and accepted as such. In contrast to this is how the person with an SUD who relapses is called a “treatment failure” and their relapse is seen as evidence that their treatment is a waste of time and limited resources. Thankfully, this mindset is beginning to shift, so that SUDs are starting to be considered chronic conditions like diabetes (McLellan, 2015).

Treatment Noncompliance²

In no other sphere of medicine is there such a social stigma attached to a failure to comply with treatment protocols. Health care professionals find noncompliance to be a source of frustration; however, it is only with the substance use disorders that noncompliance brings with it significant social stigma. To further compound the damage, noncompliance is often cited as evidence that treatment is not effective. This social stigma is expressed through comments that the client “did not *really* want to get well,” “lacked motivation,” “was only going through the motions to make a good impression on the judge,” etc.

Treatment noncompliance is an ongoing problem in all fields of medicine. It has been found that persons with a chronic illness take their medication as prescribed only 50–70% of the time (Pegler & Underhill, 2010), when adherence is generally defined as the medication being taken 80–100% of the time, at the accurate dosage (Lawrence, Miller, & Flexner, 2017). For example, older persons who are prescribed digoxin for their heart condition were found to have their prescriptions filled so rarely that it was estimated that they were taking their medication only 111 days of the year (Shea, 2006). Even patients who have received

¹Discussed later in this chapter.

²Also called *non-adherence*.

organ transplants struggle with compliance with their medications, with more than 10% not taking their immunosuppressant medication as prescribed after a lung transplant (Castleberry et al., 2017).

The problem of treatment noncompliance reflects, in part, the individual's denial and defensiveness surrounding their medical condition (Rogers, 2008). This may be further understood in light of clients' beliefs in their ability to impact their health condition by compliance. De las Cuevas, Peñate, and Cabrera (2016) found that adherence to medication is significantly impacted by this belief. Other factors that contribute to treatment noncompliance include (a) the health care provider's failure to inquire about treatment compliance, (b) improper tone during the adherence interview, (c) assumption of adherence by the treatment professional, (d) treatment professionals' attitudes toward the noncompliant individual, and (e) assignment of blame rather than reassessment and development of a new treatment approach to address the problem (Weiden, 2011).³ Surprisingly, while treatment noncompliance is of obvious importance in the treatment of various medical disorders, it is rarely emphasized in the training of most physicians (Shea, 2006). Further theory-based research will help all professionals working with noncompliance (Santiago, 2016).

Treatment noncompliance and the substance use disorders are often intertwined: Moderate-level drinkers are less likely to have prescriptions filled than are nondrinkers (Bryson et al., 2008). The authors found that only 58% of moderate and heavy alcohol users had their prescriptions for antihypertensive and lipid control agents filled, as opposed to 64% of nondrinkers (which still means that just over one-third of nondrinkers also failed to have their prescriptions for antihypertensive medications filled). Of those advised by medical professionals to enter a rehabilitation program, less than one-third follow through with this recommendation (Bryson et al., 2008). Clients who request detoxification often fail to complete the detoxification cycle because of concurrent medical problems, unwillingness to experience the withdrawal process, urges to use drugs, encouragement from others to restart drug use, etc. (Franken & Hendriks, 1999). Fareed and colleagues (2014) found, for example, that concurrent misuse of other compounds was a potent indicator of compliance with buprenorphine treatment.

While 90% of heavy drinkers could be detoxified through "social" or outpatient detoxification programs, only 70% complete the process (Myrick & Wright, 2008). Of this number, half go on to substance rehabilitation (35% of those

who enter outpatient detoxification). Although rehabilitation program professionals have not yet identified personality traits that might help in the early identification of those persons at risk for premature termination of treatment (Miller, 2003), the research has been able to identify some indications that those with externalizing characteristics may have poorer outcomes (Blonigen, Bui, Britt, Thomas, & Timoko 2016). To complicate matters, a client's willingness to enter a rehabilitation program might not reflect their level of motivation to make a major lifestyle change such as achieving abstinence (Connors, DiClemente, Velasquez, & Donovan, 2013).

Substance rehabilitation programs do suffer from significant levels of attrition. Factors such as previous social isolation, solitary drinking, not being married, having no children, and being unemployed are all associated with a higher probability of premature termination from treatment for male clients. There has been little research into the factors that might predict premature termination from treatment for women, which is discussed in Chapter 18.

Willpower

Every experienced clinician can relate at least one case history where the individual with an SUD concluded, usually but not exclusively after concluding a detox regimen, that they now feel confident that they can control their substance use disorder through willpower alone. Self-control does exist. Whether the individual's self-control will allow them to continue to abstain from chemical(s) is another question. The addictive process "brings on a slow and insidious change in desire" (Baumeister, 2015, p. 64). Over time many individuals begin to experience "euphoric recall" episodes, in which they will recall the pleasure obtained from the chemical(s) of choice, failing to remember the depths to which that chemical use brought the individual. These episodes will be intermittent and vary in strength, and for most individuals are quite mild (Baumeister, 2015). Further, willpower is a fixed, rather than an infinite commodity. The frequency and timing of these episodes contribute to a reaffirmation or an insidious breakdown of willpower. The rehabilitation counselor needs to warn the client of the nature of willpower's breakdown and use this as another reason in why external supports (pharmacological and psychological) would prove of value to the individual.

Switching Addictions

A common therapeutic belief is that if a person were to discontinue the use of one drug of misuse, they are at increased vulnerability for the development of a new substance use

³Admittedly, Weiden's (2011) article addressed noncompliance issues in the treatment of schizophrenia, but the principles appear to be equally applicable to treatment noncompliance in substance rehabilitation.

disorder involving a different substance. This is often referred to as “switching addictions” by mental health professionals. To explore the validity of this belief, the team of Blanco, Okuda, Wang, Shang-Min, and Olson (2014) carried out a prospective study involving 34,656 individuals who were interviewed 1, 2, and again 5 years after achieving abstinence. The authors found that about 20% of their research participants went on to develop a substance use disorder involving a new compound. Individuals who were misusing more than one substance at the time of admission to treatment, but who only wanted to learn how to abstain from one chemical, were more likely to switch their addiction to a new chemical. The results of this study reinforce the belief by therapists that treatment should focus on helping the individual abstain from the use of all drugs of misuse.

Lapse and Relapse

The problem of clients relapsing, or experiencing a lapse, might reflect a conflict between programmatic goals, patient goals, and the individual’s memory. Many rehabilitation programs focus only on the goal of complete abstinence; many of those in rehabilitation do not share this goal. This is seen in the finding that whereas 99% of treatment programs aspire to the goal of total abstinence, only a minority of those who graduate from substance rehabilitation treatment will completely abstain from further alcohol or drug use (Leavitt, 2003). Up to 60% of those treated for an SUD relapse during the year following their treatment program (Bowen et al., 2014). In the case of alcohol, 45–50% will have returned to their pretreatment level of alcohol consumption within a year of their discharge from treatment (Polivy & Herman, 2002). There is obviously a conflict between treatment program philosophy and treatment outcomes, as evidenced by these statistics.

Part of the problem of relapse is that substance use memories might be far stronger than the individual’s desire for abstinence. As Williams (2014) observed, “where new information conflicts with existing beliefs, our brains bend over backwards to keep beliefs intact rather than revise them” (p. 37). Thus, even in the most motivated of individuals, their brains will resist learning new information. They should be taught to expect this and taught coping strategies to help face their old beliefs and replace them with new, abstinence-based memories.

Another contributing problem is that there is no firm boundary between a lapse and a relapse, making these terms a source of endless confusion to both the lay public and rehabilitation professions. For the sake of this text, a **lapse** will be defined as when the individual initially uses a compound after a period of abstinence, such as the first puff of a marijuana

cigarette or the first swallow of alcohol. This results in a state of *abstinence violation*, and the individual reaches a decision point: Does she or he reaffirm the commitment to abstinence, or continue to use the chemical(s)? In the latter case, the individual is said to have relapsed.

The term **relapse** is drawn from the medical model, and reflects a state where the person falls back into an active disease state after a period of remission (Marlatt & Witkiewitz, 2005). Significant proportions of persons with serious medical conditions experience a resurgence of the disorder after achieving a period of stability, if not an apparent cure. Even with the best of medical care, many patients who experience a return of their disease fail to survive the relapse. In contrast, 40% of persons with an SUD eventually achieve complete abstinence from recreational chemicals either alone or with professional assistance (Gitlow, 2007). To put this figure into perspective, this rate of recovery is almost three times that seen with lung cancer (Gitlow, 2007). An additional 20% of those treated for an SUD return to periods of episodic misuse, while the remaining 40% go on to develop a progressive SUD that might ultimately prove fatal (Gitlow, 2007). This latter group forms the basis of the saying that the addictions can be arrested, but can never be cured (Gitlow, 2007).

Relapse prevention is defined as a self-management program designed to assist the individual in arresting his or her SUD to the best degree possible (Marlatt & Donovan, 2005). This may be through avoiding the actual use of substances and/or avoiding the return to attitudes or habits that might lead to use of substances (Daley & Douaihy, 2015). In this context, the individual’s relapse is not a sign that treatment failed, any more than would a diabetic person’s rehospitalization for stabilization of their medical condition would be a sign that their diabetes treatment regimen failed. However, just as there are many reasons why a treatment program for diabetes might fail, there are many reasons why the individual who is in or has completed a substance rehabilitation program might relapse. The team of Witkiewitz and Masyn (2008) concluded after their analysis of 563 individuals who had relapsed to active alcohol use that there were three different paths following the initial lapse. The first group engaged in infrequent, moderate, alcohol use. The second group were those individuals who initially engaged in heavy alcohol use, but whose frequency of alcohol use gradually became less and less frequent over time. The final group were those persons who returned to a pattern of heavy alcohol use. Surprisingly, the majority of their sample reported returning either to total abstinence or to infrequent and moderate alcohol use following their lapse back to drinking (Witkiewitz & Masyn, 2008). The authors also found that coping skills at the time of the individual’s first lapse were positively related to less frequent and less intense alcohol use at the time of relapse,

whereas more recent research has identified that a desire to control others coupled with difficulty regulating anger is predictive of lapse (Maisto et al., 2016), as well as physical pain (Witkiewitz et al., 2015).

It has been suggested that relapse is triggered by one or more of the following mechanisms: (1) drug exposure (either to the same or another compound), (2) stress exposure, or (3) cue re-exposure (environmental cues previously associated with substance use) (Boles, 2007; Clay, Allen, & Parran, 2008). Remember: Different neural circuits are involved in the initiation of substance use and those that contribute to a relapse (Leamon, Wright, & Myrick, 2008). Thus, situations that contributed to the initiation of use (and thus activation of certain neural networks) are not the same as those that might contribute to the continuance of substance use after a relapse. These are problems that must be anticipated and addressed in the latter stages of treatment.

Drug exposure may be unintentional (such as when a recovering smoker rounds a corner outside of work and encounters a cloud of cigarette smoke from coworkers). It might be the result of a prescription from a physician (for example, a former alcohol-dependent person who receives a prescription for a benzodiazepine, then relapses as a result of the similarity of effects between these two compounds). Persons used to using physicians for desired drugs might find the experience of being in a doctor's office for a necessary medical examination to be a relapse trigger (Washton & Zweben, 2006). Stress exposure is a frequent relapse trigger (Haney, 2008), and cravings have been found to be a mediator between the stress and the lapse (Law et al., 2016). It has been discovered that when exposed to significant levels of stress, men and women will activate regions of the brain that control habit-based behaviors, not those regions of the brain involved in cognitive assessment and control (Elton & Kilts, 2009). From an evolutionary standpoint this makes sense: If the source of the stress is a predator about to attack, you might not have time to make a cognitive appraisal of the situation; thus, falling back on your instincts might save your life.

Unfortunately, when faced with stress, the first response of many individuals who have misused substances might be to fall back on the habit of using chemicals to self-medicate stress, especially if they have been struggling with cravings. The individual might not adequately assess the situation, and then will select the most appropriate behavioral response, especially in the early stages of recovery. However, stress as a relapse trigger often takes unexpected forms. It is not the experience of stress that triggers a relapse; rather, the individual's loss of hope, demoralization, and depression in the face of stress appears to activate the habit-based substance use response (Elton & Kilts, 2009; Miller & Harris, 2000). If individuals believe that they have the resources to deal with

the demands being placed on them by life, they are less likely to break down under those stressors and relapse.

Social isolation⁴ and other social factors such as living with others who misuse substances can function as a relapse triggers for the individual. Interpersonal problems such as marital conflict, divorce, or child custody issues⁵ (Boles, 2007) might also serve as relapse triggers. Physical illness is a significant stressor, and often can induce thoughts of new chemical use as a way of coping with physical distress. For example, the physical sensations experienced when the person has a bad cold or influenza often are similar to the sensations of unmedicated opiate withdrawal. Unfortunately for individuals who have suffered a traumatic event, and especially those persons who have developed posttraumatic stress disorder (PTSD), intrusive, traumatic memories can serve as relapse triggers (Work Group on Substance Use Disorders, 2007).

Finally, through the process of associative learning, a large number of external cues are associated with substance use. One rarely recognized factor in relapse is the individual's sense of smell (Levin, 2008). Memories associated with smell have been found to have a stronger influence on memory retrieval than memories associated with the other senses (Konnikova, 2012). Clinically, this makes sense since human evolution has resulted in a process through which smelling something also activates memory centers. In ages past, being able to recognize the smell of a predator and then rapidly recognizing the smell as a source of danger would be advantageous. A side effect of this evolutionary adaptation in the present world is that smell might also trigger memories associated with substance use. For the individual with an AUD, for example, the smell of cigarette smoke might be associated with the experience of being in a bar where cigarette smoking is pervasive. Surprisingly, few treatment centers even mention the possibility that smells can act as relapse triggers.

Marlatt and Witkiewitz (2005) identified a number of factors that might contribute to a relapse back to active chemical use, or that might protect against such a problem:

Self-efficacy: The individual's confidence in his or her ability to cope with high-risk situations, thoughts, urges, etc.

Outcome expectancies: Individual expectations about the outcome of substance use should the person relapse. **Euphoric recall**⁶ often is activated by outcome expectancies.

⁴Which in part explains the need for participation in a substance-free support group.

⁵Such as when the state asserts that the parent is unfit to retain custody, for example.

⁶See Glossary.

Craving: Although craving in itself is a poor predictor of relapse, it might be triggered by substance use cues (sights, smells, sounds), which in turn trigger memories of past substance use. For example, a former smoker might see a cigarette that has been stubbed out in the bottom of an ashtray, initiating a craving for a cigarette.

Motivation: The individual's motivation to change, or commitment to change, plays an important role in whether she or he relapses or remains abstinent.

Coping style: This poorly understood determinant of relapse reflects the individual's ability to call upon learned coping skills to deal with substance use cues.

Emotional states: There is a strong association between substance use and relapse. Negative emotions are more often seen in cases of full relapse, while positive states appear to be more often associated with behavioral lapses.

Interpersonal support: The individual's access to a strong, substance-free, support system during times of craving contributes to continued abstinence if the individual calls upon this resource.

For each of these forces, one must also consider the proximal⁷ or distal⁸ relationship of that factor to the individual's relapse (Donovan, 2005). The individual's genetic heritage might be viewed as a distal factor for relapse (Donovan, 2005; Westphal, Wasserman, Masson, & Sorenson, 2005). A hypothetical example of a more proximal relapse trigger might be the need to have blood drawn for medical testing, where the feel of a needle entering the skin reawakens memories of past injected drug use for individuals who have misused IV drugs.

Factor analysis has yielded three categories of proximal warning signs for potential relapse (Donovan, 2005): (a) cognitive factors, (b) emotional states, and (c) behavioral characteristics of the client. These factors interact within the individual, moving him or her either closer to or further from a potential relapse. Cognitive factors have also been called maladaptive thoughts (often referred to in 12-step groups as "stinking thinking") by the cognitive-behavioral therapies (Beck, 2004; Daley & Marlatt, 2005; Keller, 2003). Examples of such maladaptive thoughts include: "I can control it

now," or "I have learned enough to avoid relapsing," or the ever-popular "I will stay out of trouble if I only bring \$20 with me to the bar. I only leave when I have spent it all." Maladaptive thoughts might allow the individual to (Beck, 2004) (a) convert normal sources of stress into excessive stress and justification for continued substance use ("I cannot *stand* to feel this way!"),⁹ (b) transform distress into craving ("I can't cope without using [X]!"), or (c) rationalize a potential relapse as being acceptable ("Surely I can handle *just one*").

Another category of maladaptive thoughts reflects the individual's desire for indulgence (Blume, 2005). Many persons view substance use as a reward for past behavior(s), thus believing "I *deserve* a drink after all that I've done!" Other persons may view substance use as a way to escape life's pressures, if only for a while. Planned or unplanned meetings with "friends" who use substances offer the individual a sympathetic ear (while he or she indulges in substance use), and thus represent a high-risk situation for a potential relapse (Blume, 2005; Westphal et al., 2005). Such maladaptive thoughts must be identified, and then the appropriate countermeasure(s) taken, to ensure the individual can remain abstinent. These examples offer an illustration as to why a substance-free support group is so important.

Many persons find that the anticipated rewards of abstinence are not as immediate as the pharmacological rewards induced by the drugs of misuse. Others, faced with life's adversities without their usual substance-based coping mechanisms, become prone to relapse. A hypothetical client who has been abstinent for 6 months only to be informed that he or she has a serious, potentially life-threatening medical problem would be hard-pressed not to at least think of returning to chemical use as a way of coping, or at least of making themselves numb to external reality, for example. A second hypothetical client who, after 6 months of hard-won recovery, returns home to be informed that his or her spouse filed for a divorce might very well wonder where the rewards of abstinence are to be found when hit in the face with such realities.

While clinical evidence has identified negative emotional states such as anger, fear, or confusion as possible relapse triggers, positive emotional states might also serve as a relapse trigger as well. The individual seeks a way to ensure that the positive feelings experienced thus far will continue. Clients thus need to learn to experience life as it unfolds, and

⁷Proximal forces are those in close temporal proximity to the event in question. For example, hitting a major pothole in the road might cause a driver to lose control of the motor vehicle, and thus is the proximal cause of the resulting accident.

⁸Distal forces are those that are more distant from the event in question. To use the example cited above, the winter's freeze-thaw cycles might have weakened the pavement, allowing the pothole to form, and eventually causing the accident discussed in the last footnote.

⁹A technique that the author of this text often calls upon when dealing with this maladaptive thought is to paint a graphic picture of \$1 million in \$20 bills. Then the client is asked whether she or he could deal with that feeling for 24 hours, at the end of which they would receive the \$1 million. If the client says "yes," it is then pointed out to the client that they have just demonstrated that they *can* deal with the stressor, and how they are responding to the stressor with addictive thinking ("I can only cope with this problem by using!"). The next step is to develop a coping mechanism to deal with that form of urge to use chemicals.

not try to control or negate it by chemical use. Negative life events happen to us all, not just to those in the early stages of recovery, although the person in the earliest stages of recovery might not understand this fact yet.

Another common cognitive error is when the client takes a short-term view of recovery rather than see the long term. If a client should remain abstinent for 6 years, she or he is less likely to relapse. Treatment staff must thus work with clients to help them understand that they must remain on their guard until recovery becomes a lifestyle, which will take a number of years to accomplish. Like many postsurgical persons, clients in the early stages of recovery must learn not to attempt tasks that they are not ready to deal with. One possible coping technique is for individuals to carry a card with the negative effects that they have experienced from their misuse of substances, and to review these consequences during a period of craving when such cognitive errors might occur. This cognitive reorientation technique will help the individual reframe a return to substance use into a negative rather than a positive event.

Social pressure was found to play a significant role in the individual's return to alcohol or drug misuse by Zywiak and colleagues (2006). The authors based this conclusion on their analysis of data from 592 enrolled in a larger research study called Project MATCH, and found three classes of relapse: (a) negative affect or family influences, (b) craving cued relapses, and (c) social pressure. The latter category accounted for more than 58% of the identified relapse events, according to the authors. They also found that motivational interviewing procedures seemed to provide greater protection against social pressure–induced relapse events than other forms of intervention utilized in the Project MATCH study.

Spiritual issues have been found to lead either back to or away from continued substance misuse (Gitlow, 2007). Such issues might include the client's ongoing feelings of shame and worthlessness, especially in the early stages of recovery. These issues might trigger (or at least contribute to) a relapse back to chemical use. Individuals who do not struggle with misuse have trouble understanding that substance use often fills a need in the individual's life. The bar, for example, might offer social contacts for an otherwise socially isolated person who fears rejection through the shared social activity of drinking. Thus, the individual's core personality is a distal relapse trigger that may predispose some persons to relapse (Chiauzzi, 1990, 1991; Donovan, 2005). Individuals who tend to have a compulsive component to their personality frequently do not react well to even minor changes in their daily routine, and substance use offers at least the illusion of controlling their anxiety. Those who struggle with dependent personality characteristics may often misuse alcohol or illicit drugs because they offer the illusion of acceptance, and have

difficulty refusing alcohol or drugs when confronted with people who offer them because of their fear of rejection.

The person with passive-aggressive traits tends to be unwilling to accept personal responsibility for their behavior and blame others for mistakes. "He offered it to me" is a common cry after a relapse. "I didn't want to be rude and not accept it!" In this manner, the responsibility is placed on the person who offered the compound in question, not on the person who relapsed. In contrast to this is the narcissistic personality. Those with narcissistic personality traits tend to view themselves as being above the rules that govern everyday society. They are generally quite self-centered, and have trouble admitting to weakness of any kind. These characteristics make it hard for them to ask for help if tempted to use alcohol or drugs. Finally, a number of personality subtypes struggle with impulsiveness, distrust of others, and rebellion. Many people view the traditional path to recovery as a form of control being imposed on them, for example. These (and other) personality types must be viewed as distal relapse triggers that must be addressed if the client is to achieve long-term recovery.

Clients with substance use disorders often, when moving toward abstinence, turn to *substitute addictions* as a way to trigger the reward pathways once engaged by the chemical(s) of misuse. Examples of such substitute addictions include the use of other chemicals. Those with an AUD might turn to beer rather than hard liquor, rationalizing this as being "safe" because of the comparatively low alcohol content of beer and the fact that they only had trouble after consuming hard liquor. Those addicted to pain medication might discontinue the use of opioids, but later admit that they have started to engage in heavy marijuana misuse. There are also endless ways that a person in the early stages of recovery might attempt to substitute another behavior for the SUD. The recovering alcoholic, for example, might turn to gambling. Helping professionals must learn to inquire about such substitute addictions.

Relapse is a process and not a single event. It is preceded by a series of subtle, often seemingly irrelevant choices known as "mini-decisions" that individually do not portend a relapse but which collectively move the individual toward this step (Keller, 2003). Few clients are sensitive to these warning signs or the dangerous mini-decisions in the earlier stages of recovery (Daley & Marlatt, 2005). A client's decision not to have a prescription for Antabuse¹⁰ refilled is a decision that appears to be innocent by itself. However, in combination with other decisions (such as participation in company-sponsored softball games where beer is available), it might ultimately lead to the individual's relapse back to active drinking.

¹⁰Discussed in Chapter 33.

Individuals in the early stages of recovery often place themselves in high-risk situations, which expose them to both relapse cues and opportunities to use again. The client might, for example, go to a bar “to hear my brother’s band play.” The desire to hear a brother’s band play is innocent enough. The setting where the band is working might present the person in recovery with a high-risk situation. One does not have to walk very far to obtain alcohol if one is in a bar, and soon the soda that one is drinking pales as the person begins to remember past drinking experiences in that environment. Other high-risk situations involve interpersonal conflict (Daley & Marlatt, 2005; Keller, 2003). A person who has just had a disagreement with a spouse, for example, may be in a high-risk situation if they were accustomed to using alcohol or drugs to cope with their angry feelings in the past. For some clients, the simple act of receiving a paycheck places them in a high-risk situation, as they now have money with which to buy alcohol or drugs.

One time of special vulnerability is the Thanksgiving/Christmas holiday season. For some persons, the stresses of being around family members, their potential alcohol use (even if on a social basis), and familial squabbles are all potential relapse triggers (Aldhous, 2009). For others, the pain of being alone over the holiday season is a potential relapse trigger. Thus, one must help the client develop coping mechanisms for dealing with the holidays without drinking or using drugs, develop alternative coping plans and skills (such as leaving the room when others are drinking, or asking that they not consume alcohol when the individual is in the room, or going to support group meetings, for example) to help the client avoid relapsing back to active use during this time of stress.

Substance rehabilitation professionals must help the client identify high-risk situations and develop the appropriate coping skill(s) to deal with those problems. This increases the client’s self-efficacy and self-confidence, although they should also be warned that this does not mean they are ready to place themselves in a high-risk situation again. A client who has been coached in alcohol-refusal skills still is not ready to go to a bar to hear their brother’s band play, for example. Temptation is just around the corner, and those refusal skills might not be up to the task even if the client should call upon them. To help the client develop skills necessary for long-term recovery from alcohol, instruments such as the Inventory of Drinking Situations (IDS-100)¹¹ may help identify high-risk situations for the person with an AUD. Staff then can help the client learn how to cope with such problem areas. A recovering friend might be asked to accompany the client to a sister’s wedding, to ensure that the client does not

TABLE 34-1 Most Common Causes of Relapse

Category	Description of Situation	Percentage of Cases
Negative emotional states	Feelings of frustration, anger, anxiety, depression, boredom, etc.	35
Peer pressure	Pressure from either a single person or a group of people (coworkers, for example) to resume the use of a chemical(s) (Tobacco, for example)	20
Interpersonal conflict	Conflict between client and a close friend, spouse, child, employer, employee, etc.	16
Craving for drugs or alcohol	Person becomes preoccupied with use of alcohol or drugs, especially in early abstinence	9
Testing personal control	Patient exposes him/herself to a high-risk situation to see whether they can resist resulting urge to use alcohol or other chemicals	5
Negative physical states	Person is experiencing illness, postsurgical distress, or acute injury, for example	3

SOURCE: Daley and Marlatt (2005); Dimeff and Marlatt (1995).

ingest alcohol at the wedding reception. Other techniques might include having the client carry a reminder card with step-by-step instructions on how to deal with the potential relapse situation, limiting the chance of a relapse. While it is not possible to identify every high-risk situation, Table 34-1 identifies many of the more common antecedents to relapse.

Bargh (2014) argued that the stronger the unconscious pushes us to engage in one form of behavior, the harder the individual must consciously work to achieve the opposite, at least at first. After repeated successes, the new conscious response replaces the older unconscious response in most situations, and in turn becomes a new unconscious response when the individual encounters a relapse high-risk situation. Most rehabilitation programs, however, do not help their clients identify unconscious triggers to chemical use so that the individual might develop conscious coping mechanisms when the need arises, although it is impossible to anticipate every possible relapse risk situation (Daley & Marlatt, 2005; Witkiewitz & Marlatt, 2004).

The research evidence supporting the concept of relapse prevention training has been mixed (Hester & Squires, 2004; Irvin, Bowers, Dunn, & Wang, 1999).

¹¹A 100-item questionnaire that will shed light on situations where the person is most likely to drink.

Dodes (2013) advocated an examination of the client's experiences or thoughts just prior to when they started to think about using chemicals again to help that person see how such thoughts or experiences trigger thoughts of abusing chemicals again. Relapse prevention programs do seem to be of value in helping the individual cope with sensations of demoralization, anger, and depression (Miller & Harris, 2000). Further, continued involvement in relapse prevention programs involving both individual and/or group therapy sessions does seem to increase the individual's chances of achieving long-term abstinence (McKay, 2006). It is even possible to integrate relapse prevention work with community-based support groups¹² to provide ongoing individual and group support for the person during times of crisis.

However, these steps are not a guarantee, and even people involved in the most comprehensive of relapse prevention programs will be at risk of slipping back into substance misuse. Unfortunately, it is not uncommon for a person who has relapsed to be referred to the same rehabilitation center where they were treated, and thus be exposed to the same treatment methods used during their earlier rehabilitation program (Fletcher, 2013). In such cases, "more of the same" might not be the most appropriate response to a relapse, and individualized treatment programs should be established.

Pain

At the risk of oversimplifying, there are two forms of pain: the acute pain that is the result of an injury, and a dull, aching, chronic pain that affects about one-fifth of the world's population for at least part of each year (Hamzelou, 2015). The symptoms of persistent pain differ from those of acute pain. It is not uncommon for persons with acute pain to describe the experience differently than persons with chronic pain. Persons suffering from acute pain will often use words such as "sharp" or "cutting" to describe their pain, while individuals with chronic pain will describe their pain as "dull" or "aching," more diffuse and with an ill-defined focal point (Jackman, Purvis, & Mallett, 2008; Smith, 2008). For generations, physicians were dependent on the patient's self-report about the intensity of both acute and chronic pain, although hopefully in the next decade scientists will develop technology to help the physician determine the intensity of the activation of those regions of the brain active in the perception of both forms of pain (Hamzelou, 2015). Unfortunately, such technology is still years in the future, leaving many individuals

and their physicians to struggle with the problem of their pain here and now.

Acute Injury

Persons with substance use disorders are often at higher risk for acute injury than nonusers. Additionally, the person with an SUD who has had a traumatic injury presents the health care professional with many therapeutic dilemmas (Woods & Bartley, 2008). For example, if an individual with an opioid use disorder should present at a hospital emergency room with a broken arm, and even after the administration of a medication that would normally provide adequate analgesia should request additional pain medication, is this person drug-seeking, or has his or her pain been under-treated?

All too often, pain is inadequately treated, even in persons with no history of a substance use disorder. Health care accreditation agencies have recognized that pain is too frequently under-treated and have made this a priority for their attention. Thus, all reports of pain should be accepted, assessed, and appropriate attempts made to address the pain (Woods & Bartley, 2008). It would be immoral for the health care professional to dismiss a person's claim that s/he is still in pain simply because "s/he is only an addict," or, in cases where the person is on an opioid agonist program, to dismiss the person's request for additional analgesic medications as irrelevant because "he [or she] is already on methadone" (or buprenorphine). This dismissal could prove rather embarrassing for the health care professional if the ever-so-casually dismissed pain was later shown to be an indicator of a potentially treatable condition.

The client's substance use history will be one of the factors that will influence the person's perception of pain following an injury. Those with an OUD who present with a fractured arm, for example, might actually require more pain medication for adequate analgesia simply because of the acquired high tolerance to narcotic analgesics and the possible development of a drug-induced state of hyperalgesia (greater sensitivity to pain) that appears to reflect opiate-induced alteration(s) in the psychophysiological pain perception system (Wachholtz, Foster, & Chearle, 2015). This fact is often unknown, forgotten, or misunderstood by health care professionals attending to the person with an OUD (Woods & Bartley, 2008).

Another danger is that the use of analgesics, even if appropriate under normal conditions, may predispose the individual to a relapse if s/he were to be recovering from an SUD, especially if opiates have been misused. Thus, issues surrounding relapse prevention must be addressed immediately after the person's stabilization. A person recovering from an AUD, for example, might find themselves re-experiencing some of the same sensations achieved by the misuse of alcohol if placed on a sedating agent such

¹²Alcoholics Anonymous, Narcotics Anonymous, or any of the other emerging secular or faith-based support groups.

as a barbiturate or benzodiazepine, even if the use of this compound is medically warranted. The similarity of effects could then trigger strong urges to use alcohol again, potentially causing a major relapse.

While this discussion is not exhaustive, it does illustrate how even those persons misusing substances might present with legitimate complaints of pain in the acute care setting. Unfortunately, such persons have also been known to abuse health care facilities to obtain desired medications. The health care professional is thus forced to engage in a very thorough investigation to determine whether the person's complaints are real or unfounded, often in a setting where s/he has limited time to address the matter. Tests such as the Opioid Risk Tool, or the Screener and Opioid Assessment for Persons—Revised, will help with this process (Jackman et al., 2008). Even without the use of these instruments, the substance rehabilitation professional must address the issue of how the person's use of a prescribed substance for what was deemed to be a medically appropriate reason might impact his or her SUD or recovery program. This is a complicated matter, which varies from person to person, and within the same person over time.

Chronic Pain

Chronic pain can be defined as pain that lasts for more than 3 months (Hamzelou, 2015), although others indicate that it is pain that is more than 6 months beyond the time period that would be anticipated for healing (Miller & Frankowski, 2012). Estimates are that between 10 and 20% of the general population in the United States live with a non-cancer-related persistent (or chronic) pain disorder (CPD) (Nahin, 2015; Porreca & Price, 2009; Smith, 2008). Persons with substance use disorder histories are not exempt from chronic pain. Some of those who struggle with a chronic pain disorder will have a concurrent substance use disorder, which complicates the treatment of each disorder. Unfortunately, there is evidence that persons with mental health or substance use disorders are more likely to receive prescriptions for narcotic analgesics than persons who do not suffer from such disorder (Braden et al., 2010; Edlund et al., 2010). To further complicate matters, even the person who does not have an SUD may find that his or her pain is no longer controlled at what was once an effective dosage level of a narcotic analgesic. It had been hypothesized that the brains of persons who experience severe chronic pain treated with narcotic analgesics might undergo subtle changes that ultimately might make the person more pain-sensitive, although it is not known whether this possible alteration in brain function is permanent (Borsook, 2010; Miller & Frankowski, 2012; Smith, 2008). This appears to

reflect the phenomenon of **pseudo-addiction** or **neuroadaptation** to the medication's effects, an expected phenomenon often seen with prolonged use of narcotic analgesics (Miller & Frankowski, 2012). In this type of situation, the demand for more medication does not, as many health care professionals fear, reflect an SUD. Rather, the process reflects neuroadaptation. Once the person's pain has been adequately addressed, they usually do not make demands for additional pain medication(s). Their vocal demand for additional pain medications, however, is very similar to that of a person misusing substances who desires more narcotic analgesics for personal gain. The physician must discriminate between the legitimate needs of the former group of persons, while avoiding the administration of unnecessary drugs to the latter group.

Even compliant persons with an SUD may become pain-sensitive because of acquired partial tolerance to the pain medication(s) being administered (Chang, Chen, & Mao, 2007; Compton & Athanasos, 2003). This can be seen in the observation that extended treatment with methadone causes the individual to become pain-sensitive (Chang et al., 2007). To avoid having to deal with the complex issues of possible opioid misuse as opposed to legitimate requests for additional medication for analgesic reasons, some physicians believe that it is useful to withhold narcotic analgesics from persons with concurrent SUDs. There is little evidence to support this therapeutic myth. The essential question is whether the dosage of a narcotic analgesic being administered is sufficient to provide an appropriate level of analgesia in the physician's opinion.

Even under the best of conditions, CPD can be quite refractory to medical treatment. The individual's expectations are a major factor in the success of pain management. Many persons hope that the right medication(s) will provide complete pain relief, which might be an unrealistic expectation (Borsook, 2010). This can contribute to feelings of hopelessness, depression, and possible suicidal thinking by the person, who desires a way of escaping from what they view as a hopeless situation. Other persons might adopt a pain-centered coping style, limiting their exposure to situations that might cause or exacerbate their pain. While the person views these adaptations as useful, they often cause long-term disruption to the person's life and hold the potential to exacerbate their pain over time (Smith, 2008).

Persistent pain disorders are a challenge to medical professionals, many of whom have little or no training in working with patients with these problems. The percentage of physicians who have had training in the treatment of chronic pain in persons with a substance use disorder is quite small. This is not always an easy task, especially

since persons with an SUD and who also have a persistent pain disorder are a very difficult subpopulation to work with, even under the best of conditions. Health care professionals working with such individuals often fear medication misuse or diversion, or the possibility that prescribed treatment might exacerbate the person's substance use disorder (Compton & Athanasos, 2003; Miller & Frankowski, 2012). Many physicians respond to this dilemma by simply refusing to treat persons with these co-existing disorders.

Miller and Frankowski (2012) identified several criteria that should suggest to the clinician that the individual might be misusing his or her medication: (1) deterioration in work performance, (2) involvement in illegal activities, (3) alteration of route of administration, (4) multiple episodes in which the individual reports "lost" or "stolen" prescriptions, (5) refusal to comply with toxicology testing, (6) concurrent misuse of other compounds, (7) use of multiple pharmacies or physicians, (8) requests for medication beyond that which would normally be necessary for pain control for their condition, (9) unsanctioned dosage escalation, and (10) nonadherence to the entire pain treatment program (which might include physical therapy, etc.) but continued use of narcotic analgesics. If a person has been discharged from another pain-management program for noncompliance, this should raise the clinician's suspicion about similar behavior by the client in the present setting (Miller & Frankowski, 2012). Finally, inquiries about what medications/dosages other patients are receiving, or justification for dosage increases because another person is receiving a higher dose of a certain medication, are also significant red flags suggesting possible medication-seeking (Miller & Frankowski, 2012).

To assist the attending physician in making a determination as to the appropriate medication decisions, a treatment team that works together closely, is in constant contact, uses consultations with appropriate treatment professionals when needed, and the use of a treatment contract are of value (Miller & Frankowski, 2012). It is important that the physician be clear that the use of the opioids will be discontinued if at any time risks seem to outweigh the benefit for pain relief (Dowell, Haegerich, & Chou, 2016). The treatment contract will specify that the person must (a) use only one specified pharmacy, and only one doctor (except in emergency situations) (Miller & Frankowski, 2012). In the latter case, Miller and Frankowski (2012) recommend the person-physician contact must be reported to the person's care coordinator within 72 hours so that the treatment team can determine whether there was a legitimate need for the person to see another doctor. They recommend the treatment contract should also specify that the person will be required

to submit to urine toxicology testing on a random basis at least once every 6 months,¹³ and that they will be called back for "pill counts" to make sure that they are taking prescribed medications per instructions.¹⁴

The treatment contract should state that the person understands that non-opioid treatments such as physical therapy, or non-opioid pharmaceuticals (gabapentin or valproate, for example), as well as psychosocial support and lifestyle changes (dieting, exercising, etc.) will be utilized as indicated (Cheatle & Gallagher, 2006; Jackman et al., 2008). Unfortunately, rural health care professionals rarely have access to treatment teams such as the one outlined above, and must face the problem of treating those with chronic pain in their home communities. Still, the person should be expected to sign a treatment contract such as the one outlined above, clearly specifying that failure to adhere to the provisions of the contract are grounds for termination of treatment.

A fear among physicians treating those struggling with pain with narcotic analgesics is that the continued use of these medications will induce an addiction. It has been suggested that younger males and those who have access to a larger supply of medication that they can take without medical supervision are at highest risk for developing an opioid use disorder related to medication misuse (Edlund, Steffick, Hudson, Harris, & Sullivan, 2007). To combat these problems, having the pharmacy dispense the medication in smaller lots (such as every second day), employing a trusted family member, or in smaller communities having the person report to the physician's office to have the medication(s) dispensed by the office nurse are all options.

It is imperative for health care professionals working with individuals who have or are misusing substances and also have persistent pain to understand that the lifestyle of these individuals often makes them intolerant of incomplete solutions, or of lengthy treatments. "I want what I want, and I want it *now!*" is the mantra of a large percentage of these individuals, forcing the medical staff to establish boundaries almost immediately and to rigidly enforce them. A violation of the treatment contract by a person who "only wanted some more pain relief" by taking nonprescribed medications should be considered grounds for termination of treatment. Once the word is spread that a given chronic pain program expects cooperation and will enforce program rules, there will be fewer such cases to deal with.

¹³The urine toxicology test should utilize technology to detect synthetic and semisynthetic narcotics often not detected by less sophisticated tests. This topic is discussed in more detail elsewhere in this chapter.

¹⁴A person who should have 18 pills of a specified medication left when called back for a pill count but who only has 12 pills in the bottle should raise suspicions that he or she is either taking more than was prescribed, or is diverting medication.

Some physicians may advocate the use of a long-term opioid agonist, such as methadone, for the treatment of chronic pain disorder (CPD). The long therapeutic half-life of methadone reduces the possibility that the individual will experience “breakthrough” pain, which is a common problem when other narcotic analgesics with shorter therapeutic half-lives are used. However, about 37% of patients on a methadone maintenance program will report experiencing a CPD, while 60% will report some level of pain even while on methadone maintenance (Barry et al., 2009). There is virtually no clinical literature on how to assess or address these problems in the patient on methadone maintenance programs, although evidence would suggest that the treatment of coexisting psychiatric problems (depression, etc.) will often reduce the patient’s pain intensity (Barry et al., 2009).

While the narcotic analgesics are the mainstay of treatment of acute pain (<16 weeks), the effectiveness of such compounds for longer periods of time (>16 weeks) is in dispute (Blondell & Ashrafioun, 2008). Additionally, there have not been studies on the benefits for long-term (a year or longer) use of narcotic analgesics (Dowell et al., 2016). The Centers for Disease Control and Prevention (CDC) recommends that non-opioids be the preferred choice for chronic pain, and that opioids should only be used when the benefits outweigh the many risks (Dowell et al., 2016). Compounds such as the tricyclic antidepressant medications, anti-epileptic medications, serotonin-norepinephrine reuptake inhibitors, and the nonsteroidal anti-inflammatory inhibitors (NSAIDs) can be used either as the primary modality of treatment for CPD or at least as adjunctive treatments for chronic pain (Ananth, Richeimer, & Durham, 2012).

Research data to guide the clinician in working with these special patients is lacking (Morasco et al., 2010). More research is needed on CPD, especially since it is logical to assume that this problem will become more common. It has been suggested that patients’ pain be treated by an integrated treatment team of professionals from various professions (nurses, psychologists, etc.) rather than by physicians alone (Azar, 2011), and that this would help minimize but not eliminate the problem of physician manipulation by those misusing substances seeking additional medication while providing optimal control of the individual’s pain.

Controlled Drinking

In contrast to rehabilitation programs in England, where the majority of all alcohol rehabilitation programs offer assistance in helping clients learn how to moderate their drinking, in the United States the concept of “controlled” drinking has met with skepticism. Unfortunately, ever since the first preliminary research studies were published suggesting that

it might be possible for individuals with AUDs to learn to control their drinking, many persons with a severe alcohol use disorder have seized on this as justification for their continued alcohol use. If they should encounter problems and engage in heavy drinking, they will say they are still in the process of learning how to “control” their drinking and simply need to work harder at this goal.

The concept of controlled drinking has been challenged in the research literature. Miller, Walters, and Bennett (2001) suggested that only 10% of test subjects were able to remain controlled drinkers over a span of 12 months following discharge from treatment. Other studies have found that the long-term success rate in achieving and maintaining long-term controlled drinking is less than 2% (Vaillant & Hiller-Sturmhofel, 1996). Controlled drinking is perhaps a viable goal for individuals who are not physically addicted to alcohol, have a shorter drinking history, and who have not encountered significant psychosocial problems as a result of their alcohol use disorder. However, research has found that “stable moderate drinking [is] a rare outcome among treated alcoholics” (Wallace, 2003, p. 19). Persons with more severe alcohol use disorders rarely remain moderate or controlled drinkers, but rapidly return to their abusive drinking patterns, according to the research data, and Morgan (2006) warned against a goal of controlled drinking for this subgroup of drinkers. Yet more recent research has found that abstinence-based treatment and controlled-drinking treatment are similarly effective, and when individuals are given the option of choosing goals, the success of treatment is greater (van Amsterdam & van den Brink, 2013).

This conclusion is supported by a study by the team of Adamson, Heather, Morton, and Raistrick (2010), who found that the client’s stated goal of desiring to learn how to control their drinking as opposed to abstinence was a predictor of long-term success. Persons who worked toward abstinence were more likely to be abstinent than those who wanted to be controlled drinkers 3 months after treatment (22% were abstinent, while only 13% were controlled drinkers, according to the authors). The authors also found that after 12 months, 44% of those persons who had stated that their goal was controlled drinking had achieved this goal, in contrast to the 71% of those persons who had worked toward abstinence. However, many of those whose initial goal was controlled drinking shifted their goal toward total abstinence after encountering problems or losing control of their drinking.

Allowing the person with an alcohol use disorder to attempt to return to controlled drinking is often a useful goal in the person’s ultimate rehabilitation. A failed attempt at returning to controlled drinking helps the client realize that abstinence is a more viable goal for him or her than attempting to return the social use of alcohol. However, the treatment

professional needs to weigh the potential benefits of this experiment against the possible risks, and document in the clinical record that the client was warned of the risks inherent in their attempt to return to controlled drinking, including the fact that only a minority of those who attempt this are able to maintain long-term controlled drinking as opposed to relapsing back to misuse of alcohol.

Early Recovery and Sexual Activity

It is important for health care professionals to recognize that persons with an SUD might have learned to associate the use of certain compounds (such as cocaine, for example) with sexual activity. Through associational learning they might have come to believe that “normal” sex involves the use of these chemicals, and find that intimacy is not as rewarding without the use of these chemicals (Gitlow, 2007). Other persons might find interpersonal intimacy rather uncomfortable without using a chemical(s), possibly because of feelings of inadequacy or social anxiety. Still a third group of those misusing substances have been the victims of sexual assault at some point in their lives, and they have learned to use the **anxiolytic**¹⁵ effect of alcohol, marijuana, or other compounds to make themselves numb to the feelings reawakened by sexual contact.

For all three subgroups, interpersonal intimacy without the use of alcohol or drugs might prove to be frightening. Indeed, some persons will have misused alcohol or illicit drugs for so long that they have no memories to guide them in a relationship without a chemical in their system. For example, a hypothetical 50-year-old father of three children might report that he has not been intimate with his wife for the last 15 years of their marriage without having some alcohol in his system, and that he is afraid of possibly being rejected by her.

For all three subgroups of those misusing substances, interpersonal intimacy might serve as a relapse trigger. It is not unusual for clients to keep these fears to themselves, in large part out of shame, or be unwilling to discuss them with an opposite-sex therapist. A referral to a therapist of the same sex who will then assess the role that alcohol or drugs have played in the person’s sexual activity would be appropriate, and appropriate referrals to a licensed, experienced sex therapist, individual psychologist, social worker experienced in marital therapy, etc. should be made.

“Cravings” and “Urges”

It is interesting to note that in spite of the importance attached to the concepts of drug use “cravings” or “urges” by substance rehabilitation professionals, there is no standard definition of either term, nor is there an objective way to measure either construct (Anton, 1999; Ciraulo, Piechnczek-Buczek, & Iscan, 2003; Ekhtiari, Nasser, Yavari, Mokri, & Monterosso, 2016; Kavanagh et al., 2013; Weiss et al., 2003). Different researchers use the same terms in different ways, contributing to confusion not only among professionals but also in the popular media about the experience of a drug-use thought and a relapse.

A drug-use thought is just that: a thought. A client who, at the end of a hard day’s work, might think that “a cold one [beer] would be nice now” has just experienced a drug-use thought. The experience is transitory, as are all thoughts. Clients should be taught that such drug-use thoughts are normal, especially in the early stages of recovery. These thoughts are the result of associational learning. In the hypothetical example cited above, the client might very well have learned to associate a beer with the end of the work day. In such a case, having such a thought is normal. *Acting* on that thought is inappropriate. We all have thoughts, and if the truth be told we all occasionally think about doing some inappropriate things (“I wonder what it would be like to rob a bank?” for example). Most of us do not act on those thoughts.

Drug **craving** is an intense, subjective, emotional, and physical experience for the individual, that varies in intensity between individuals. Some individuals might find that they are responding as they normally would if they were about to use a chemical(s), such as having sweaty palms, anxiety, increased heart rate, and possibly increased salivation, or the other physical sensations that they came to associate with substance use. They focus almost compulsively on drug-use cues, and may view themselves as being overwhelmed by these feelings. Neurologically, this experience has been explained as parallel to the reduction in glutamate receptor sites in the nucleus accumbens region of the brain in the early stages of recovery, as well as blood flow changes in the brain’s reward system (Tapert et al., 2003; Weiss, 2005). However, the ever-changing field of neuroscience is now pointing toward complex networks within the brain that explain cravings (Ekhtiari et al., 2016).

Thus, drug cravings are the subjective event (that we may someday be able to map with brain imagery!) experienced while the brain adapts to the absence of the drug(s) of misuse during the early stages of recovery. The craving might be triggered by an internal stimulus (a thought or physical sensation, for example), or an external drug-use cue (seeing a used hypodermic needle in the gutter, for example). These

¹⁵See Glossary.

drug-use cues trigger a subjective experience of craving in the individual. Unfortunately, because of the process of neuroplasticity, urges become stronger if the individual should give in to them even once, since neural pathways (and associated receptor sites) increase when used (Schwartz & Beyette, 1996). The reverse process, extinction, will require that the brain rewire itself, a process that takes time. During this process, the individual will experience cravings and urges to return to the use of chemicals.

Surprisingly, since craving for a chemical is a subjective experience, the same symptoms of craving might be interpreted as intense by one person, as moderate by a second, and as quite weak by a third person (Weiss et al., 2003). The experience of craving waxes and wanes in intensity during the first 12 weeks of abstinence, and the client should be warned that their craving will be most intense during this period (Carol, Smelson, Losoczy, & Ziedonis, 2001). However, clinical experience suggests that after the first 90 days, the individual's experience of craving will become less intense, and less frequent, feedback that might offer the client some hope to cling to during the early days of recovery.

It is important to keep in mind that there is a vast difference between a hard choice to abstain from chemicals, and no choice but to use those chemicals (Gendel, 2006). Urges and cravings are not the same as obligations to use alcohol or drugs (Heyman, 2009). Such cognitive experiences are just part of the early recovery phase. Clients should be warned to expect them, and they should be trained in how to respond to them.

The “Using” Dream

A common phenomenon that needs further research is the “using” dream. These dream experiences may be quite frightening to the person in the early stages of recovery. Lewis (2011) spoke about how “using” dreams contributed to a relapse back to opiate use disorder on his part: The dream memories would cause him to ruminate about opiate use until he could not stand it any longer and felt that he had to fulfill the desire with actual drug(s). Other clients will report having awakened after a dream in which they used drugs or alcohol that was so intense and seemed so real that they had trouble separating reality from the dream experience for the first few seconds after awakening. Such dreams may make the client wonder about his or her commitment to recovery. As noted earlier, they might also be a relapse trigger by themselves. It is thus important to warn the client that these dreams are both common and usually not a sign of impending relapse. These dreams are also important information that can be used in treatment to help rather than hinder recovery (Miller, DiCicco, Fox, & McCourt, 2015).

There are two types of dreams: (a) the rapid eye movement (REM) dream, which accounts for most of our dream experiences, and (b) the non-REM dream. Dreams that take place during REM sleep are sometimes noted for bizarre, intense imagery that often makes no logical sense: A long-dead relative walks through the wall in the dream, and the dreamer simply asks, “Would you like some tea?” (Doweiko, 2002). Non-REM dreams tend to be rather dull, and involve the dreamer carrying out routine tasks, with little emotional content.

During both REM and non-REM dreams, there is a neuromuscular blockade that prevents the body from acting on motor movement commands generated by the sensory motor region of the cortex during sleep. The brain's production of **acetylcholine**¹⁶ drops significantly during dream sleep, which appears to be part of the psychomotor blockade that develops during REM sleep. If awakened, the dreamer may recall vague sensations of not being able to move normally, intense emotions, and confusing, often irrational thoughts.

Another process that seems to take place during the REM dream is that the brain practices the fight-or-flight response. Dreaming is a safe time to do this, since the body is unlikely to act out on the motor movement commands involved in the fight-or-flight response. During REM dreams the **amygdala**¹⁷ is exceptionally active, a fact that supports this theory. These fight-or-flight response emotional memories are intense sensations of fear and anxiety, feelings that might carry over into the dream's waking state for a few seconds.¹⁸ In the normal waking brain, it is the duty of the cortex to make sense of internal and external sensations, and if the dreamer is feeling fear, then there must be something in the dream experience that initiated that fear. Memories of substance misuse would certainly cause the dreamer to feel anxious if they were committed to abstinence.

The outcome of these two processes is that (a) the dreamer has vague memories of not being able to move naturally in the dream, memories that may closely simulate their experience(s) while under the influence of chemicals. Also, (b) the dreamer recalls feeling anxious, if not very frightened during the dream state as the brain's neurochemical balance shifts from the dreaming state to the waking state. A relapse would be a situation that could trigger such intense emotions. Fortunately, **anticipatory guidance** (a fancy term for helping the client anticipate that certain experiences might happen to them, so that they might mentally prepare for them) will help

¹⁶See Glossary.

¹⁷See Glossary.

¹⁸A process called *dream carry-over*. Through this experience the dreamer continues to experience emotions generated during the dream for the first few seconds of consciousness.

the client deal with such dreams. Further, as the associational memories between substance use and various substance-use cues weaken over time, these “using” dreams will generally become less intense and less frequent over time. It seems rare for a client to report such dreams after the first 3 months of recovery, although on rare occasions clients will report such dreams and as having awakened with the thought on their minds: “Why would I ever want to do that again?”

Toxicology Testing

Urine¹⁹

The issue of urine toxicology testing is one of the more controversial issues in the field of substance rehabilitation. Appropriate urine toxicology testing must balance the factors of (a) the method of sample collection for analysis, against (b) comprehensiveness (range of compounds being tested for), (c) speed at which test results will become available to assessor(s), (d) sensitivity of test procedures to detection of specific compounds, (d) the possibility of false positive findings, and (e) cost. The discussion of the method of sample collection must begin with urine toxicology testing. This procedure is relatively noninvasive, painless, and allows for on-site urine sample collection. However, there are a variety of urine toxicology testing procedures, each of which offers benefits and liabilities to the assessor.

Most on-site urine toxicology tests allow for the testing of a large number of urine samples simultaneously at relatively low cost, and the results are often available in minutes. However, the results are reported only as either positive or negative, and many commonly misused drugs are not detected by these tests (Craig, 2004; DuPont & Selavka, 2016; Franklin, 2012). This characteristic of on-site urine test results might lead the assessor into a sense of false security since many assessors assume negative results mean that there was no evidence of substance use detected. In reality, a negative finding only suggests that there was no evidence of the use of those compounds that the test was designed to detect.

For example, although they are both classified as narcotic analgesics, a quick test designed to detect evidence of morphine use is unlikely to detect evidence of fentanyl misuse. Further, these tests require that the metabolites of the drug of misuse be present at specific concentrations (called

the **detection threshold**) before the test is classified as positive. Remember that the body is actively attempting to biotransform all foreign molecules, and thus the concentration of the metabolites of a specific compound will change over time. If a test requires that drug molecules for a hypothetical substance A be present at 50 mg/deciliter of urine for a positive result, and the actual concentration is only 30 mg per deciliter of urine, the test will provide a negative result because the concentration is below the detection threshold.

With some types of urine toxicology tests, structural similarities between certain compounds may result in false positive test results, a process known as **cross-reactivity** (Collins, 2009; Craig, 2004). Through this process, the reagent used to detect one class of illicit chemicals reacts to another, possibly unrelated compound. An excellent example of this is that on some tests the use of the cough suppressant dextromethorphan at therapeutic doses may result in the person being identified as a phencyclidine misuser (Mozayani, 2009; Traub, 2009). If a false positive seems likely, further testing will be needed to secure accurate information (Sadock, Sadock, & Ruiz, 2015).

“It is important to keep in mind,” Collins (2009) observed, “that cross-reactivities and interferences may change with reagent lot changes, new formulations and variable antibody specificity” (p. 31). Further, physical disease states such as **proteinuria**, nitrites, ketones, or blood in the urine, as well as bacterial and fungal infections, can cause nonspecific cross-reactivity between these compounds and the immunoassay procedure being used (Collins, 2009). Thus, the process of cross-reactivity is not static, and it is the responsibility of the laboratory to stay informed as to the variables that might affect the test outcome with each of the reagents utilized on an ongoing basis.

False positive test results are a significant problem with the relatively unsophisticated on-site test kits used by many employers, parents, and law enforcement officials. Some of these tests have a false-positive rate of 30–35% (Schuckit, 2006a, 2006b; “Why confirmatory testing is always a necessity,” 1997). It is because of such false positive test results that confirmatory testing should always be carried out. Methods such as *gas liquid chromatography* (GC) are useful at this stage of the assessment process. Gas liquid chromatography is a more expensive, and labor-intensive, procedure that requires the use of expensive laboratory equipment operated by specially trained technicians. The GC procedures require time for completion and do not lend themselves to rapid screening of large numbers of urine samples. In spite of the disadvantages, GC tests have a lower risk for false positive results, and provide the assessor with quantitative levels of the chemical(s) detected in the individual’s urine (Craig, 2004).

¹⁹The information provided in this section is designed to illustrate the known strengths and weaknesses of toxicology tests. It is not intended as, and should not be used as, a guide for prosecution, treatment, or employment sanctions.

Other procedures, such as the *gas chromatography/mass spectrometry* (GC/MS) test, might also be called upon to confirm a positive urine sample from a less sensitive test procedure. GC/MS is very labor intensive, expensive, and limited to testing only a small number of urine samples at a time. One advantage of GC/MS procedures is that they can detect a wide range of individual substances, reducing the risk of false positive results. In the example cited earlier, the hypothetical person who had used the cough suppressant dextromethorphan at therapeutic doses will have the dextromethorphan molecules in the urine sample identified as such and not as phencyclidine. Because of this specificity, GC/MS results may be introduced as legal evidence of illicit drug use in many states.

However, individuals using illicit drugs and companies attempting to produce appropriate testing procedures are involved in an arms race of sorts (Jones, 2009). Many companies sell products that can break down metabolites produced by illicit drugs over time. Also, if too much time should pass between the immunoassay test and the GC/MS test, the initial test could suggest drug use, while the GC/MS test indicates no evidence of illicit drug use because the test-defying chemical finally had time to work (Jones, 2009). Even if the individual had not attempted to alter the test results, urine toxicology procedures will not detect signs of illicit drug use until at least 6 hours after the individual's use of a compound since the body needs time to begin the biotransformation and elimination processes before urine toxicology testing can detect evidence of substance use (Juhnke, 2002).

Urine toxicology testing is more complicated than obtaining a urine sample and submitting it for analysis. Most states require the client's written consent to the urine toxicology testing process; many states require that strict chain-of-evidence procedures be followed and that the results be interpreted only by a trained medical review officer (MRO). Such a review of test results should address the ongoing myth that a positive urine toxicology test indicates impairment (Stein & Rogers, 2008). Insurance companies and employers argue that even the smallest trace of a drug in a person's urine after an accident is evidence of impairment and thus grounds for job termination, legal action, etc. Such a stance ignores the reality that substance-induced impairment cannot be inferred just because toxicology testing suggests that a given compound was present in the individual's body (Reisfield, Goldberger, Gold, & DuPont, 2012). It is impossible to determine substance-induced impairment solely on the basis of drug concentration levels in body fluids, other than for alcohol, for which there is an extensive research database demonstrating levels of impairment at various blood alcohol levels (Jemionek,

Copley, Smith, & Past, 2008; Reisfield et al., 2012; Stein & Rogers, 2008). Reisfield and colleagues (2012) suggested that by the very nature of these substances, such determinations remain only an illusion.²⁰

As is evident in the material reviewed thus far, urine toxicology testing is controversial and fraught with the potential for misinterpretation,²¹ even by medical professionals. In spite of these problems, urine toxicology testing provides the assessor with one source of data about the individual's possible substance use.

CLIENTS' ATTEMPTS AT DECEPTION

It is not uncommon for clients misusing substances to attempt to manipulate the urine toxicology test to avoid having recent illicit drug use detected. These attempts at detection avoidance generally fall into one of three categories (Jaffe, 2010): (a) *in vitro adulteration*, in which the test subject adds a prohibited chemical to the urine sample to hide evidence of recent drug use; (b) *in vivo adulteration*, in which the test subject ingests a compound prior to testing (including the simple ingestion of large amounts of water) to dilute or disguise signs of illicit drug use; and (c) *urine substitution*, in which the test subject substitutes a negative urine sample for one known to be positive. Another means of test manipulation is to simply not keep a scheduled appointment if the client has reason to anticipate being asked to submit to urine toxicology testing at a given time ("I have to work, honest!" or the ever-popular "My car won't start!") (Gitlow, 2007).

In vitro urine toxicology test deception methods rest on the assumption that it is possible to hide evidence of illicit drug use by adding a foreign chemical to the urine sample. A partial list of adulterants used at one time or another to disguise urine samples tainted with illicit drug metabolites includes those listed in Table 34-2. It should be noted that when Drano® or salt is added to the urine sample, there is a high probability of undissolved crystals being suspended in the sample, at least a first. This will assist in the detection of tampering if the urine sample is closely examined as soon after collection as possible.

²⁰As was discussed in the chapter on CNS Stimulants, there are cases where one individual has become toxic on a therapeutic dose of an amphetamine, whereas another individual might be using a dosage level far above the therapeutic range without signs of amphetamine toxicity, for example.

²¹Reisfield et al. (2012) pointed out, for example, that a valid prescription for a controlled substance was an affirmative, but not absolute, defense against an impaired driving charge. However, should the individual demonstrate clinical signs of impairment, he or she could be charged with driving while under the influence of mood-altering substances even though it was a prescribed medication, according to the authors.

TABLE 34-2 Sample List of Agents Used in Attempts to Hide Drug Use

Ammonia
Bleach
Blood
Drano®
Ethanol eye drops
Gasoline
Kerosene
Lemon juice
Liquid soap
Peroxide
Vinegar
Table salt
Sodium bicarbonate
Vitamin C

In vivo methods of urine toxicology test deception include compounds designed to bind with the drug metabolite, altering its chemical structure so that it does not register as an illicit substance. There are also a number of products that are used to remove toxins from the body, or to correct electrolyte imbalances induced by the client's attempts to flush their body with large amounts of fluids (Coleman & Baselt, 1997; Gwinnell & Adamec, 2006; Jaffe, 2010). Some persons have been known to ingest large amounts of water in an attempt to flush drug metabolites from their body, or at least dilute the drug metabolites to a level that will fall below the detection level, a process that exposes the individual to the risks inherent in water intoxication.²²

On rare occasions, the ingestion of such compounds to modify a urine sample will actually hide evidence of recent illicit drug use, although they also alter the chemical characteristics of the urine sample submitted (DuPont & Selavka, 2016; Schuckit, 2006a, 2006b). Some compounds will make the urine sample more alkaline than is possible for human urine, for example (Jenkins, Tinsley, & Van Loon, 2001). Small amounts of the compound alum will hide metabolites of methamphetamine in a urine sample, but at the cost of changing the acidity of the sample, which can be detected by treatment or laboratory staff when they check the sample's acidity level. If possible, the specific gravity, acidity level, and creatinine levels of the urine sample submitted should be assessed to determine whether a given urine sample is appropriate for testing or has been altered through

such methods (Coleman & Baselt, 1997). These adulteration methods do work under certain circumstances, and health care professionals might wish to consult with toxicology laboratories to determine which compounds might work with the specific method of drug testing being used, and how their use might be detected.

Another method by which individuals who use illicit drugs might attempt to manipulate the urine toxicology test results is by urine substitution. This is a method of deception through which individuals will substitute other compounds for their urine. A partial list of compounds submitted as "urine" by various clients includes apple juice, citrus-flavored sodas, diluted tea, ginger ale, lemonade, salt water, plain tap water, peach tea, and white grape juice. Again, testing the sample's specific gravity and acidity level (as well as the amount of sugar in the sample!) will detect these attempts at substitution.

People have also been known to attempt to substitute a "clean" (i.e., drug-free) urine sample, possibly hidden in a balloon or small bottle, that can be substituted for their own urine sample if nobody is watching closely. This is easily done in most cases, since the majority of urine toxicology test samples are not collected under supervision (Sutheimer & Cody, 2009). Even if urine samples for toxicology testing are collected under supervision, there are companies that will sell a rather realistic-looking artificial penis, so that the male client might submit a substituted urine sample even while being observed. The urine is held in a storage container that is squeezed, forcing it through a tube and into the collection bottle, just as would occur if the man were to submit normally to urine toxicology testing. A similar device is sold for females. If done properly, the results are very realistic. An extreme method of deception is a urine substitution method through which a client will void their bladder, then insert a catheter and fill their bladder with another person's urine to provide a urine sample for testing if asked²³ (Stein & Rogers, 2008).

Clients who have been asked to submit to urine toxicology testing have been known to claim to be unable to urinate when somebody is watching them in an attempt to avoid supervised urine collection, or to "accidentally" dip the urine sample collection bottle into the toilet water. The specific gravity and level of acidity of the urine sample will reveal this attempt at deception, since toilet bowl water has a different specific gravity and acidity level than does human urine. Some treatment centers add a coloring agent to the toilet water to foil these attempts at substitution. Further, toilet

²³This process, however, exposes the individual to all of the risks inherent in using a catheter, and to potential infectious organisms in the urine of the person who supplied the urine sample to be substituted.

²²Including, but not limited to, cardiac arrhythmias and cerebral edema.

water is usually rather cool when compared with the human body, and urine is always within 1–2 degrees of the core body temperature if the temperature of the urine sample were to be tested within 4 minutes of the time that it was collected (Katz & Fanciullo, 2002). This fact is embarrassing to those clients who attempt to simulate normal body temperature in the substituted urine sample by putting the sample into a microwave oven prior to reporting for toxicology testing. Temperature testing at the time of collection will thus help to identify urine samples that are unusually warm or cool, alerting staff to possible attempts at deception.

Urine toxicology testing should be carried out on a random basis (Juhnke, 2002). Some court-associated outpatient programs assign a color to each client, who must then call a central telephone number to see whether clients with that color will be called in for urine testing that morning. In residential programs, a client might be selected at random and told that he or she is to report for urine toxicology testing, and is then escorted to the collection site so that the client does not have time to sneak into their room and pick up a chemical or urine substitution sample. The information reviewed below provides an overview of the detection windows for various compounds commonly misused.²⁴

ALCOHOL

Under normal conditions, a client will only show traces of alcohol in their urine for about the same time as it can be detected on their breath. Thus, breath analysis is the preferred method of detecting alcohol in a person's body, although later confirmatory testing in a certified laboratory might be carried out by law enforcement officials. Recently a urine toxicology test for alcohol was introduced to detect a metabolite of ethyl alcohol known as ethyl glucuronide. This compound is specific to alcohol use, and remains in the individual's blood for up to 5 days after the person's last drink. Unfortunately, there is a growing body of evidence suggesting that exposure to alcohol through such things as hand sanitizer²⁵ might also cause a positive test result (DuPont & Selavka, 2016; Kirn, 2006). Given the popularity of such products, the results of the ethyl glucuronide test must be interpreted with caution.

AMPHETAMINE COMPOUNDS

In the casual user, amphetamine compounds might be detected for 24–48 hours (Bolnick & Rayburn, 2003; Greydanus & Patel, 2005; Schuckit, 2006a). However, high doses of ephedrine or pseudoephedrine might cause a false positive test result. For this reason, federal guidelines require

that amphetamine molecules be identified through specific testing procedures such as the gas liquid chromatography (GC) test (discussed above) in order to rule a urine sample positive for amphetamine compounds such as methamphetamine. In the case of methamphetamine, it is important to keep in mind that once the chemical is ingested, the body breaks methamphetamine down into amphetamine, but ephedrine or pseudoephedrine are not biotransformed into this compound. This allows the presence or absence of amphetamine or methamphetamine to be confirmed by the appropriate test procedures after the initial test results suggest amphetamine use.

BENZODIAZEPINES

Depending on the specific benzodiazepine being used, urine toxicology tests might reveal evidence of benzodiazepine use for 1–4 weeks after last use (Craig, 2004). Schuckit (2006a) suggested a shorter detection window of only 3 or more days. This discrepancy appears to reflect whether one is testing a rare misuser of a benzodiazepine, or a chronic user. The benzodiazepine Rohypnol (flunitrazepam) is technically a member of the benzodiazepine family of compounds, but it is not legally available in the United States. Routine toxicology tests will not detect it, although special tests can detect it in a urine sample if the test is carried out within 60 hours of the time that it was ingested. These tests are usually available only to law enforcement agencies investigating date rape claims.

COCAINE

Depending on the route of administration, the frequency with which the individual uses cocaine, and the amount of cocaine used, it is possible to detect metabolites of cocaine in urine for 72–96 hours (Craig, 2004; Jenkins et al., 2001; Schuckit, 2006a). Individuals who use heavily might continue to test positive for cocaine metabolites for up to 10 days after their last use of the compound (Traub, 2009). Greydanus and Patel (2005) suggested that individuals who use cocaine chronically could test positive on urine toxicology screens for up to 2 weeks after their last use of the compound, while Schuckit (2006a) simply stated that chronic users would test positive for “several days” (p. 30) after their last cocaine use.

One of the exceptions to this rule is when the person is using a prescribed product with traces of cocaine in it, such as certain skin lotions. If the person were to be using one of these compounds, this could produce a false positive test result. Fortunately, these skin lotions are available only by prescription, and thus it is rare for this situation to arise (Ahrendt & Miller, 2005). Passive absorption of cocaine is possible for a physician or dentist, if their practice brings them into frequent contact with this compound, in which case they will have metabolites of cocaine in their urine for

²⁴This information is provided for illustrative purposes only, and is not intended for, and should not be used as, the basis for employment screening, legal, or other purposes.

²⁵Many brands of hand sanitizer contain ethyl alcohol.

72–96 hours (Gitlow, 2007). Fortunately, it would be relatively easy to determine whether that health care professional's job duties did indeed bring him or her into frequent contact with cocaine.

LSD

LSD might be detected in a person's urine for up to 8 hours after it was last used, but the laboratory must use special testing procedures to detect this substance (Craig, 2004).

MARIJUANA

Although the cannabinoids have been the most commonly detected illicit substances in urine toxicology tests for more than 20 years, the detection of marijuana through urine toxicology testing remains rather complicated (Huestis, 2009). The excretion of marijuana metabolites from the body is variable, but correlates well with the amount of marijuana used by the individual (Goodwin et al., 2008). Rare social users will have traces of THC in their urine for 3–5 days after they last used marijuana (Goodwin et al., 2008; Greydanus & Patel, 2005; Schuckit, 2006a). There is a persistent myth on the streets that those who smoke marijuana will have traces of THC in their urine for 30 days after their last use of marijuana, and casual users will often repeat this myth as if it were gospel to try and avoid sanctions for illicit substance use.

Individuals who smoke marijuana daily or more often will build up significant THC reserves in their bodies, which will leak back into the blood through osmosis for between 20 and 45 days, depending on the frequency with which they used marijuana and the potency of the marijuana smoked (Greydanus & Patel, 2005; Jenkins et al., 2001). Those who participate in exceptionally heavy levels of marijuana smoking have been known to have measurable amounts of THC in their urine for up to 2 months after their last use ("Weight loss and the release of THC from fat," 2009).²⁶ Katz and Fanciullo (2002) suggested that an individual who habitually smokes marijuana might test positive for THC for up to 80 days, although this figure has not been supported by other researchers.

Many individuals who use marijuana test positive for marijuana for such extended periods because THC enters the body's adipose tissues and is slowly released back into the circulation after the individual stops marijuana use. To avoid controversy, it has been suggested that the client submit to daily urine toxicology testing until his or her urine sample fails to show evidence of marijuana use for 3 straight days. The program staff must make sure that the person does not have a prescription for compounds such as Marinol®, which

is a form of synthetic THC used to treat chemotherapy-induced nausea, as this will register as marijuana on urine toxicology tests.²⁷

Occasionally, clients will attempt to claim that they have THC in their system as a result of passive inhalation. Passive inhalation of enough marijuana smoke to allow the individual to absorb sufficient marijuana smoke to test positive on urine toxicology testing has been called "extraordinarily unlikely" (Ahrendt & Miller, 2005, p. 962). However, it is possible to passively inhale enough marijuana smoke to test positive for it on a urine toxicology test. To do so it is necessary to sit in an airtight chamber so filled with marijuana smoke that the person will need swimmer's goggles to protect his or her eyes from the irritating effects of the smoke ("Oral fluid drug testing," 2005). The authors suggested that since most motor vehicles or houses are not airtight, the claim of passive inhalation is not supported by the evidence. Rohrich and colleagues (2010), using a different methodology, reached essentially the same conclusion.

MDMA

Ecstasy can be detected for 24–48 hours after it is used, but special urine toxicology testing must be carried out to detect it (Craig, 2004).

PCP

In the individual who only uses rarely, phencyclidine can be detected for 48–72 hours after it was last used (Jenkins et al., 2001). Craig (2004) offered a detection window of 2–8 days for such individuals, and up to 21 days for someone who uses PCP chronically. Depending on the testing methodology utilized, some over-the-counter medications can cause false positive reactions, and thus confirmatory testing should be carried out to confirm the initial test results (Ahrendt & Miller, 2005).

Hair Sample Testing

Whenever a person ingests a chemical, molecules of that substance are circulated throughout the body. In many cases, molecules of that compound are then incorporated into the body's cells, including the hair cell follicles and ultimately the hair. Scientists have developed technology to detect drug metabolites of many illicit drugs in the hair of the user. It has been suggested that since this is true, the collection of hair samples would be less intrusive than collecting urine samples,

²⁶It should be pointed out that "measurable amounts" is not the same as THC levels above the detection threshold utilized by the Department of Transportation to identify individuals actively using marijuana.

²⁷One favorite trick of some individuals is to obtain a blank prescription sheet and have a friend fill out the form as if it were a standing order for Marinol. If their marijuana use is then detected by a toxicology test, they can show the prescription sheet and claim that it was the prescription drug that was detected, not illicit marijuana. Thus, such prescriptions should be verified with the physician who supposedly prescribed the Marinol if THC is detected in a urine toxicology test.

and much more difficult to falsify. Hair samples also offer a detection window of seven up to 100 days (DuPont & Selavka, 2016; Gwinnell & Adamec, 2006; Stein & Rogers, 2008; Sutheimer & Cody, 2009). This extended detection window foils any attempt by the drug user to avoid detection by abstaining from drug use for a few days before a urine toxicology test (Craig, 2004). Although some individuals think they can foil this process if they shave their heads, any body hair can be used for such tests.

Advocates of hair follicle testing point out that this procedure is far less intrusive than urine toxicology testing. However, there have been several challenges to the use of hair for toxicology testing. The Food and Drug Administration (FDA) has warned that several of the test kits sold might result in false positive test results on occasion ("FDA revised guidelines, label warnings," 2004). Further, initial positive results should be confirmed by a second test that utilizes a different methodology (Sutheimer & Cody, 2009). One study found that in 60 out of 100 individuals tested, the preliminary positive results for opiate use were not supported by confirmatory testing ("FDA revised guidelines, label warnings," 2004). Further, fully 50% of the preliminary positive results for amphetamine use, 10% of the preliminary positive results for marijuana use, and 2% of the preliminary positive results for cocaine use were found to be false positive results upon confirmatory testing.

Since some individuals who use marijuana will often claim passive exposure to marijuana smoke as an explanation for positive test results, Uhl and Sacks (2004) suggested that the test try to detect metabolites other than THC, such as 11-nor-delta-9-tetra-hydrocannabinol-9-carboxylic acid (THCA) to differentiate between actual marijuana use and passive exposure to marijuana. This metabolite is produced only when the person has used marijuana, not through passive exposure, and for this reason hair samples from persons just exposed to marijuana smoke failed to reveal evidence of THCA when tested (Uhl & Sacks, 2004). This discovery will allow individuals who actually used marijuana to be identified, and foil their claim of passive exposure to marijuana smoke.

Detractors of the process of hair testing point out that a number of hair strands must be removed. Craig (2004) suggested that as many as 40–60 hair strands be removed. Further, it is hard, if not impossible, to detect when the individual indulged in illicit drug use. In theory, hair grows at the rate of 1 centimeter (cm) per month, which if true would allow the tester to estimate the time since the user last used the compound. Questions have also been raised as to whether this estimate of hair growth rate is the same for all ethnic groups (Gitlow, 2007; Sutheimer & Cody, 2009). Further, at any point in time, 15% of hair follicles

are either in a resting phase or ready to fall out, factors that can potentially influence the accuracy of hair toxicology testing. Hair toxicology tests cannot detect substance use in the 7 days prior to the collection of the hair samples, and they do not detect alcohol use (Gwinnell & Adamec, 2006; Juhnke, 2002). Research has found that different laboratories often provide different results for the same hair sample (Sutheimer & Cody, 2009), and there is no standardization in hair collection and preparation procedures between laboratories. These observations raise questions as to the validity of hair sample toxicology testing (Stein & Rogers, 2008; Sutheimer & Cody, 2009). Additionally, hair will often not show use unless the person has used at least four times in a given month (DuPont & Selavka, 2016). For these and other reasons, the federal government has discontinued the practice of testing hair samples to detect illicit drug use ("How long does cocaine remain in the hair of former users?," 2009) for job sites where such testing is mandated.

Even if evidence of illicit drug use is detected in hair strand testing, this does not provide information on the level of impairment caused by the individual's drug use (Juhnke, 2002; Stein & Rogers, 2008). The fact that hair toxicology testing requires the removal of hair from the body, as opposed to the collection of urine, a waste product expelled from the body, makes it of limited value in serial toxicology tests (Craig, 2004). Thus, there are strong objections to the use of hair toxicology testing, making its applicability uncertain at this time.

Saliva

Another emerging technology is the use of saliva to test for traces of alcohol or drug use. New techniques make this procedure attractive for workplace drug testing programs, not least because it is minimally invasive. There are a number of variables that must be resolved before the accuracy of saliva drug testing can be established, since "saliva flow can . . . be decreased due to menopausal hormone changes, stress, smoking, anti-cholinergic drugs that inhibit [the] parasympathetic nerve impulses, anticonvulsants, and tranquilizers" (Moore, 2009, p. 206). Saliva toxicology testing is also hampered by a smaller detection window than is possible with urine toxicology testing (Moore, 2009). The test results are available in approximately 20 minutes, and, depending on the substance, might offer a detection window of 1–36 hours (Dolan, Rouen, & Kimber, 2004; Stein & Rogers, 2008). The individual to be tested must be observed for 30 minutes before the test is administered to ensure that there is no attempt to dilute possible drug residue by stimulating the production of saliva. As with any screening procedure, confirmatory testing is necessary to rule out false positive results.

Sweat

A number of companies offer skin patches impregnated with compounds designed to react to and reveal evidence of illicit drug use. Such detection devices are useful for continuous monitoring of the individual over a 1- to 14-day period (Kadehjian & Crouch, 2009; Stein & Rogers, 2008). The sweat drug detection patch is designed to allow passage of water molecules, while stopping the larger drug molecules that have diffused into the sweat from the circulation (Kadehjian & Crouch, 2009). However, illicit drug use will not be detected for several hours after the individual used the compound since it requires time for drug molecules to diffuse into the sweat glands.

To avoid detection, some individuals will remove the skin patch the day it is applied, and then reapply it 6 or 7 days later, when they report to their probation officer, employer, etc., to have it removed. Such tampering is evident to the skilled patch user since the patch is designed to separate internal membranes from the outer shell if it is removed before being examined (DuPont & Selavka, 2016; Kadehjian & Crouch, 2009). While some clients might claim that their skin naturally produces oils that will cause the patch to fall off, or that it just fell off while they were taking a shower, it is extremely unlikely that the patch will just fall off on its own. Further, while clients might claim that the patch tested positive for one or more substances because of environmental contamination, research has shown that this is virtually impossible except under specialized laboratory conditions (Kadehjian & Crouch, 2009). The nature of this test method does not allow for retesting if positive or borderline results are obtained, since by the time that the test results are available, metabolites of the initial drug use would no longer be in the individual's sweat. This delay also would make confirmatory testing through other test methods difficult, if not impossible.

Blood

Given that blood has the smallest window of detection (typically less than 24 hours) and testing is considered quite invasive as well as expensive (DuPont & Selavka, 2016) blood testing is generally not seen in many treatment settings or in aftercare. It is much more frequently seen in medical settings related to testing after overdose, or in law enforcement situations such as after an accident (DuPont & Selavka, 2016).

Funding

Imagine that you had a form of cancer: You call your insurance company representative to determine whether you have coverage for potentially life-saving surgery. When you speak to the customer service representative on the telephone, you

are informed that while your insurance policy does appear to include such surgery as a covered expense, this is not a guarantee of payment for the surgery. Or consider this second, equally hypothetical, scenario: You have been diagnosed as having the same form of cancer, but when you check with the customer service representative at the insurance company's home office you are told that your policy only will pay for the first 10 days of a 30-day chemotherapy regimen, or perhaps not pay anything toward a chemotherapy regimen on the grounds that the pharmaceuticals involved are still classified as "experimental" by the insurance company. Or consider a third hypothetical scenario: Your health care insurance provider informs you that they will pay for a portion (or all) of your treatment expenses only if you enter a program at what they call a "preferred provider," the effectiveness of which is suspect.

The money that the insurance company must spend paying for health care for policyholders is considered a financial loss (or an operating expense) for that company's shareholders. The insurance company thus attempts to maximize inflow of money, while limiting payments distributed. One way to do this is to exclude many persons from receiving an insurance policy because they had a "preexisting condition." Another way to limit losses is to avoid identification of persons with disorders. To this end, only 34% of insurance companies required that the physician screen for substance use or mental health disorders when doing a physical examination (Horgan, Garnick, Merrick, & Hoyt, 2007). If the insurance company will not reimburse for a specific part of the examination, the physician is less likely to carry it out, increasing the chance that the client's mental health or substance use disorder will not be detected. Interestingly, recent research has shown that despite insurance being provided to more people through the Affordable Care Act of 2010, admissions to SUD treatment have declined by 11% since the act was implemented (Saloner, Akosa Antwi, Maclean, & Cook, 2017).

Mental Health Parity Laws

Funding dictates the form and duration of treatment. In an ideal world, the level of care offered to an individual with a substance use disorder would be determined solely by need. In reality, decisions about treatment are often shaped by funding. The middle class is caught between making too much money to qualify for public treatment funding and an inability to pay for extended treatment services "out of pocket" (Fletcher, 2013; Leamon et al., 2008). Striking a fair balance between the need for the treatment of substance use disorders and funding availability has proven difficult.

Students are thus surprised to learn that, in spite of the widespread media attention paid to the passage of "mental health 'parity' laws," health care insurance

providers are not required to provide funding for mental health or substance use treatment. The law requires that they pay for substance use treatment at the same level of reimbursement as other covered medical disorders if the insurance policy includes coverage for mental health and substance use rehabilitation programs.

Surprisingly, 77% of all substance rehabilitation programs are paid for by public funds, which are drawn from state-funded programs that are a part of the criminal justice system in that state, the Medicare and Medicaid programs, or on the federal level by the Veterans Administration treatment system (Stewart & Horgan, 2011). Services are paid for either by the fee-for-service or the fixed budget system (Stewart & Horgan, 2011). Neither system of payment is perfect. In the fee-for-service system, reimbursement is based on units of service provided, such as the number of group or individual therapy hours provided to the individual in treatment. This can serve as an incentive for a for-profit rehabilitation program to offer a large number of more expensive ancillary services to increase revenue (Stewart & Horgan, 2011).

In contrast to this, the fixed budget system involves a contractual agreement that is reached between the payer and the treatment provider(s), in which a fixed fee is paid to the provider independent of the number of referrals made or the intensity of treatment necessary. For example, a hypothetical county might pay an equally hypothetical treatment program \$100,000 to provide substance rehabilitation services for that county for 1 year. That fee is then paid to the rehabilitation program even if only two individuals are referred to the program in the fiscal year. Of course, if 1,000 individuals are referred to the rehabilitation program in a fiscal year, the county still only reimburses the program \$100,000! Such programs thus have a financial incentive to maximize profits by eliminating ancillary services provided (Stewart & Horgan, 2011).

These forms of reimbursement are found in privately funded,²⁸ publicly funded, and third-party payor (such as by health care insurance) reimbursement situations. Health care insurance providers have attempted to hold down the cost of substance rehabilitation through a variety of mechanisms, the most notorious of which is called *managed care* (MC). Managed care has essentially been called medical rationing by accountants, and it can be argued that the needs of the individual are subservient to the company's desire to save money (Black & Mann, 2009). Frequently decisions about the services that will be reimbursed are governed not by client-centered, risk-benefit calculations, but by company focused cost-benefit algorithms. The patient's quality of care

becomes subservient to the company's desire to make money. In far too many cases, rapid, cheap *symptom reduction* (not resolution of the problem) is the goal because this saves the company money. It also applies a system of "rigid protocols with a preset, algorithmic approach" (Nasrallah, 2010a, p. 14) to the treatment of human beings. In some cases, funding for treatment is so limited that further funding is cut off before the individual has completed the detoxification cycle for the drug(s) of misuse (Fletcher, 2013)! This is especially true for older persons with an alcohol use disorder who require longer to withdraw from alcohol than do younger drinkers.

In the time since managed care (MC) programs were introduced, it has become clear that this is a system that rations health care access in all but name (Sanchez & Turner, 2003). Many health care providers have started to refer to "managed care" as "managed profits" because of the way the system limits the amount of money distributed by insurance companies for designated services. As Nasrallah (2010a) observed, "The not-so-hidden agenda of the business-oriented managed care systems is to lower costs, not to provide the best personalized medical care" (pp. 13–14). Some MC programs utilize a *preferred provider* system in which clients' level of coverage for services provided is higher if they are seen exclusively by a provider who is part of their referral network. Often the preferred provider has signed an agreement with the insurance company to reduce charges for their services in anticipation that the greater volume of clients will offset any potential revenue loss. Another system by which MC companies attempt to control expenses is through a *capitation payment* system, in which services for an individual are reimbursed up to a predetermined limit. If the provider is able to accomplish the desired treatment goals for less than this limit, the program will make money. If the expenditure to reach treatment goals exceeds this limit, the program will not show a profit. Obviously, if the program should wish to survive in today's economic climate, they must hope to make a profit, and so there is an incentive for the rehabilitation program to limit the length of stay and intensity of treatment (Stewart & Horgan, 2011).

Unfortunately, in spite of research findings that indicate that the longer a given individual is involved in treatment programs, the more likely they will abstain from alcohol or drugs, authorization for treatment stays of 14 days or less have become the norm (Ceren, 2003; Daley & Marlatt, 2006; Olmstead, White, & Sindelar, 2004; Simpson, 2004). Finally, managed care programs aggressively push for pharmaceutical treatment of identified conditions rather than behavioral treatments (Breggin, 2008). Some health care insurance providers include a capitation provision in insurance policies sold, limiting the number of admissions for detox or treatment admissions to a pre-set limit, possibly only one such admission in the person's lifetime. Such reimbursement

²⁸On rare occasions, a person might pay for treatment out of pocket.

programs have been found to cut the cost charged to the insurance company while doing little to change long-term health care risks for the clients (Nasrallah, 2010a). It is not known how mental health parity laws will change this practice, or even if it will change this practice.

Many MC companies demand that rehabilitation programs follow “evidence-based” treatment protocols. Unfortunately, much of the research on which evidence-based treatment is based are of little value in the real world. One research study might specify only persons who are male, in treatment for the first time, between the ages of 21 and 34, and who have no concurrent physical or mental illness. Such practices are defended on the theory that these confounding variables would make interpretation of the study results meaningless. Unfortunately, treatment rehabilitation center staff must work with clients who have glaucoma, diabetes, AIDS, a history of head trauma, multiple prior treatment admissions, and who might also be depressed or suffer from schizophrenia, not the pristine research samples on which evidence-based treatment is carried out. Even research carried out through the Veterans Administration (VA) hospital system is atypical, because only those people who have successfully completed active duty in the armed forces are entitled to use the VA system for health care.

Another way for insurance companies to limit financial loss is to limit treatment to *symptom reduction*. To accomplish this, the insurance company adopts a very liberal interpretation of what is considered “recovery.” Is the person still having delirium tremens? Is their blood pressure still elevated? If not, she or he should be ready for discharge in the next 24 hours, right? If you wish additional time, you will need to obtain *prior authorization*. Although research has demonstrated that older drinkers might require up to 30 days to completely detoxify from the effects of long-term alcohol misuse, insurance company benefits often are limited to 5–7 days for detoxification and treatment

unless authorization is obtained for a longer stay in treatment. Such treatment extensions are then subject to review, usually every second or third day, with the goal of ending further insurance funding once the client reaches a certain minimal set of criteria. While such policies might be considered cost-effective by the insurance company, a sad consequence of this process is that many clients are referred to aftercare before they have finished detoxification.

Chapter Summary

Even after a given client has been identified as being in need of either outpatient or inpatient substance rehabilitation, the obstacles facing the substance rehabilitation professions are often daunting. Some clients will challenge the accuracy of the diagnosis, or the accuracy of urine toxicology test results. Some may come to treatment sessions under the influence of chemicals. Even if the client consents to treatment, his or her health care insurance provider must be contacted, and prior authorization obtained for the treatment program, and continual justifications must be provided for treatment beyond the limited number of days that the insurance company authorizes.

Treatment noncompliance is an ongoing problem in a wide range of medical conditions, but if a person misusing substances should be noncompliant, the medical profession often just labels the person as being a hopeless alcohol or drug addict, and turns away. Even if the client successfully completes treatment, there are obstacles facing the client, including relapse cues and triggers, and prejudice by health care providers toward persons with SUDs. Although treatment staff may recommend extended aftercare programs for the client, many resist such recommendations, or fail to actively participate in such programs. There are other obstacles facing the client, which were discussed in this chapter.



CHAPTER 35

Support Groups to Promote and Sustain Recovery

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 35.1** Understand the history of support groups for recovery
 - 35.2** Identify the most commonly encountered support groups for recovery
 - 35.3** Understand the purpose of the various support groups identified
 - 35.4** Review the 12 steps of AA
 - 35.5** Consider the effectiveness and challenges of 12-step and other support groups
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*Introduction*¹

For many years, Alcoholics Anonymous (AA)² had a “near exclusive dominance” (White & Nicolaus, 2005, p. 59) as a community-based support group for those who had an alcohol use disorder. It has been estimated that 95% of substance rehabilitation programs utilize some kind of 12-step group model similar to that offered by AA, and that recovering center staff are quite uninterested in treatment approaches that do not utilize such an approach (Brigham, 2003). Professional support is quite strong for 12-step-based approaches, as evidenced by the observation by McPherson, Yudko, Afsarifard, and Freitas (2009), who suggested that participation in 12-step groups is an essential element in recovery.

However, in the past few decades there have been a growing number of secular support groups that reject many of the core elements of the AA program, offering alternatives for those who feel uncomfortable with the spiritual emphasis on the traditional 12-step group movement,

¹In earlier editions of this text, the 12 steps of the AA program were included as part of the chapter introduction. Permission to do so was kindly granted by Alcoholics Anonymous World Services, Inc. The 12 steps have since been moved to Appendix 3.

²Over the years, the membership of AA has evolved from one in which the members exclusively misused alcohol to one where the member usually has a substance use disorder involving multiple substances. However, because the AA program was originally designed for persons with an alcohol use disorder, this focus will be retained when discussing Alcoholics Anonymous.

for example. In this chapter, we will briefly examine the role that self-help groups play in the recovery from a substance use disorder.³

The History of Alcoholics Anonymous

There were many diverse forces that were to blend over time to form the organization that was to become known as Alcoholics Anonymous (AA). First, there was the social atmosphere in the United States, which has traditionally placed great emphasis on public confession, contrition, and salvation through spirituality. These were elements of a nondenominational religious movement that was known as the Oxford Group, which also came to influence the evolving self-help group. Finally, there was the attempted psychoanalysis of an American who was an alcoholic by Carl Jung. The former was especially influential, providing the AA movement with a strong belief in free will and personal responsibility (Committee on Addictions of the Group for the Advancement of Psychiatry, 2002).

Historically, AA is thought to have been founded on June 10, 1935, the day that a physician identifying as an alcoholic had his last drink (Nace, 2005a). Shortly before this, the physician, Dr. Robert Holbrook Smith ("Dr. Bob") had a meeting with a stockbroker, William G. "Bill" Wilson,⁴ who was struggling to protect his newly established sobriety while on a business trip to a new city. After making several telephone calls to various people he hoped might help him, somebody suggested that he talk to Dr. Smith, who was actively drinking. He did so, but rather than ask for support in his own struggle to abstain from alcohol, he began to talk about why he wanted to abstain from alcohol. At the end of the meeting, he concluded that he now understood why he made the original decision to quit drinking and thanked Dr. Bob for listening. The self-help philosophy of AA was born from this moment.

At first, AA struggled to find itself, as evidenced by the fact that within the first 3 years there were only three AA groups and only a scattering of success stories. But the fledgling movement continued to grow slowly, and by the fourth year of its existence there were about 100 members in

isolated AA groups (Nace, 2005a). To guide the newcomers, those early members who had achieved abstinence decided to write of their struggle to abstain and to share their discoveries with others. These reports were then compiled into the first edition of the book *Alcoholics Anonymous*, published in 1939, now called the "Big Book" of AA. The organization continued to grow, and there are now approximately 57,900 AA "clubs" in the United States and some 115,000 located in 150 different countries around the world (AA World Services, 2014; Fletcher, 2013). Perhaps 5 million people in the United States attend a self-help group because of alcohol or drug use disorders at least once each year (SAMHSA, 2008).⁵

Elements of AA

There are several elements that contribute to the effectiveness of a self-help group such as AA, not the least of which is that it is freely available to all (Ries, Galanter, & Tonigan, 2016). Further, such programs are widely available, as noted above. Additionally, many meetings are "closed" to all people but those who have an honest desire to stop drinking. There are three types of closed meetings: (1) The first type of closed AA meeting is a discussion meeting. The group leader has identified a topic applicable to the recovery program for all members (getting along with others, for example), which is discussed at the meeting. (2) The second type is a general meeting, a "speaker" meeting, in which members are encouraged to discuss their recovery programs, problems that they might have encountered, what is working for them, and so on. (3) The third type of closed meeting is a step meeting, in which one of the 12 steps is identified, and the whole focus of the meeting is on that step and how it applies to every member, their understanding of that step, and so on. Some AA groups rotate through the 12 steps every 3 months, whereas other groups devote an entire month to each of the steps. There is no established protocol for how to carry out step meetings.

Another aspect of AA that enhances its effectiveness is that all people involved have shared the same problem. By definition, a self-help group is just that, a self-help group, and as such it should be self-governing. It does not attempt to provide formal psychotherapy, but through example and feedback offers an educational experience for the participant. Self-help groups place great emphasis on individual responsibility for one's problems in a person who has made a personal

³A health care provider might assume a degree of liability when referring a specific individual to a self-help group. Salzer and Kundra's (2010) paper provides an excellent overview of this issue. Health care providers should consult an attorney in the state(s) in which they practice to become aware of the specific liabilities they assume when making a referral to a self-help group.

⁴As a historical side note, Bill Wilson rejected the disease model of alcoholism.

⁵Although these statistics appear to be in conflict with each other, the former statistic discusses *active* members in AA, whereas the latter statistic addresses how many people attend a self-help group in a given year, including those who attend only one meeting that year.

commitment to change (Committee on Addictions of the Group for the Advancement of Psychiatry, 2002). To this end, the individual must choose to participate in the group process. Self-help groups place great emphasis on anonymity, a factor that separates it from social groups. Finally, there is only a single purpose to the group, which again differentiates it from social groups. The early members of AA freely borrowed from the fields of religion and medicine to mold a program that worked for them, the famous 12 steps, which form the core of this self-help movement.

There are also “open” meetings. Open meetings may be speaker meetings or discussion meetings, which any interested person can attend, with no expectation of active participation placed upon those who attend. One or two volunteers will speak about how the program helped them abstain from alcohol, and visitors are encouraged to ask questions about AA and how it works. For some people with an SUD, attending an open meeting is less threatening as a first step into recovery than going to a closed meeting. After attending one or two open meetings, the individual is then encouraged to begin to attend closed meetings for personal growth.

A Breakdown of the 12 Steps

At the core of AA are the 12 steps.⁶ These steps are not required for members, but are suggested as a guide to how a person might achieve lasting recovery (Beazley, 1998). A central tenet of AA is that individuals’ resources alone are inadequate to help them abstain from alcohol. It is only through a commitment to a support group that people are able to draw upon the strength of the entire group in their battle to abstain from alcohol (Davison, Pennebaker, & Dickerson, 2000; “How Alcoholics Anonymous works,” 2007). In this sense, AA might be viewed as functioning as a form of folk psychotherapy that aids personal growth through a series of successive approximations toward a better life. The 12 steps might be viewed as these successive approximations.

New members are not encouraged to seek the cause of their alcohol use disorder (AUD). The problem is the individual’s current drinking. “It is not so much how you came to AA, as what you are going to do now that you are here,” one hypothetical member might say to a newcomer. New members are not admonished for relapsing. Members in AA know that this is an ever-present danger. However, it is the goal of the group to offer individuals a new lifestyle that they hopefully will adopt in place of their alcohol-centered former lives. The 12 steps are one guide to this transition.

In the process of following the 12-step program, the individual will encounter the first of many paradoxes: The first step is the only one that mentions alcohol by name (although Step 12 does mention “alcoholics”). This step asks the individual to make a conscious choice to admit that she or he is powerless over alcohol at the deepest level of his or her being. This requires a difficult choice, for it requires great humility and an admission of defeat in the sense that people must admit that they have been unable to deal with their AUD on their own. However, to accomplish this, people also must make a choice to view their best “friend” (alcohol) not as a solution but as the problem. The 12 steps guide individuals through this process.

The 12 steps fall into three groups, the first of which includes Steps 1–3. These steps focus on helping the individual make a profound choice: first to confront the social stigma associated with the addiction; second, to accept that this disease does affect the individual; and third, to admit that the individual is powerless over alcohol. Included in the first three steps is the act of surrendering and turning one’s life over to a “Higher Power” of the individual’s choice. Through the act of admission to powerlessness, the individual opens the door to emotional support from other, more experienced members (Felices, 2012). Individuals are also asked to remove themselves from their self-appointed role as the center of the universe and accept that there is a Higher Power. The only requirement for a Higher Power is that it indeed be something greater than the person. Programs that suggest that a doorknob, for example, could be a Higher Power serve only to belittle the 12 steps and the individual. By turning one’s life over to a Higher Power, one moves alcohol from the center of one’s mental arena, a place that normally should be occupied by one’s Higher Power. The first goal of the new member in this phase is simply to abstain and to establish a relationship with the Higher Power of his or her choice.

Steps 4–9 are a series of change-oriented procedures designed to help the individual (a) identify, (b) confront, and (c) ultimately overcome the personal character shortcomings that are thought to support the individual’s addiction. These steps allow the individual a mechanism through which he or she might work through the guilt that arises from past misdeeds and recognize the limits of personal responsibility. The individual is encouraged to develop a recovery-oriented support system, something that is often alien to the person in the early stages of recovery and also to the family of that person. The person learns the disease theory of alcoholism as AA uses the term, the mechanism by which to find help (sponsor, recovering friends, and so forth), and the means to access help when needed (calling one’s sponsor, a friend who is also in recovery, and the like). Guilt felt by the individual for past alcohol-centered behavior is hopefully replaced by a sense of

⁶In Appendix 3.

gratitude for assistance offered, and the learning of new ways of living. It is during this phase that individuals must identify and then face resentments for past harm that they have suffered, and learn to let go of these resentments and forgive the person who caused this harm.

Finally, Steps 10–12 challenge the individual to continue to build on the foundation established in earlier steps. Part of this process includes a continued search to identify additional personal shortcomings, which are then addressed by the person. The person has also hopefully learned to suspend judgment about others and to beware of the false pride that could lead back to a relapse. Spiritual growth continues to be encouraged, and finally, in step 12, the individual is encouraged to carry this message of hope to others.

Although the AA program is designed to aid spiritual growth, this process is not rapid. Indeed, the foundation of spiritual defects on which alcoholism is said to rest is resistant to change, and the process of rebuilding the self can take many years. Beazley (1998) suggested that the individual must remain actively involved in AA for at least 5 years to allow the process of spiritual growth to proceed. However, once this process is started, individuals begin to wonder how they could possibly have lived otherwise. This is the promise held forth by proponents of Alcoholics Anonymous. The 12 steps are not forced on any member. Rather, they are offered as a guide to assist the person in a program of spiritual growth, and there are those who insist that the 12 steps were instrumental in saving their lives.

The Relationship Between Alcoholics Anonymous and Religion

One complaint often voiced by those people who are resistant to participating in AA is that they do not like the religious aspect of the program. For some people, this complaint is a convenient excuse not to participate in an AA group. For others, this hesitancy reflects individual confusion over the manner in which the words *faith*, *religion*, and *spirituality* are often used interchangeably. There are very real differences between these words. Religion is an organized set of beliefs that are encoded in certain texts considered sacred by believers and are viewed as providing answers to life's questions by those who belong to that faith community (Ameling & Povilonis, 2001). Faith is viewed as the expression of belief in the face of ever-present doubt.

Although the following quote is quite old, it does illustrate that within the AA program, alcoholism is viewed as a "spiritual illness, and drinking as a symptom of that illness. The central spiritual defect of alcoholics [is] described as an excessive preoccupation with self. . . . Treatment of

the preoccupation with self is the core of AA's approach" (McCrary & Irvine, 1989, p. 153). Within this framework, compulsive alcohol use is viewed as the opposite of true spiritual growth, and it has been found that there is a strong relationship between spirituality and abstinence from alcohol (Nace, 2005a; Robinson, Cranford, Webb, & Brower, 2007). In contrast to the focus on alcohol as the person's answer to life's problems, true spirituality is a reflection of the individual's search for meaning in life and placing one's "self" into a relationship with a transcendent power. The difference between religion and spirituality is, unfortunately, a source of endless confusion for those who view AA from the outside, and those who are just starting the journey to recovery.

The difference between spirituality and religion was perhaps best summarized by McDargh (2000), who observed that "religion is for those who are afraid of going to hell . . . spirituality is for those who have already been here [as a result of their SUD]." Within this context, it is possible to view the person with an AUD as having found a Higher Power in alcohol (or, by extension, the other drugs of misuse) (Ringwald, 2002). Twelve-step programs seek to assist the individual to switch from the Higher Power of alcohol to a more benign one (Wallace, 2003). It is through this process that AA presents itself as a program for spiritual growth, but not as a religious movement (Vaillant, 2000; Wallace, 2003). To better understand this point, it is helpful to view religion as the form, whereas spirituality is the content of belief. The spiritual aspect of the AA program helps the new member to "let go," a concept that many newcomers find confusing. However, "having faith is not a question of clinging to a particular set of beliefs, a particular set of . . . practices or psychotherapeutic techniques. Having faith . . . requires that we let go of what we are clinging to" (Rosenbaum, 1999, p. xii).

This is, perhaps, most clearly seen in the inverse relationship between prayer and alcohol use, for in prayer one reaches out to a Higher Power and with humility establishes a relationship with that Power (Lambert, Fincham, Marks, & Stillman, 2010). This in turn will assist individuals in learning how to correct their distorted perception(s) of how to deal with conflict, relate to others, or have fun without the use of alcohol.

The AA program is not forced upon the individual, but the 12 steps are suggested as a road to recovery. Participation in AA requires that the individual at least be receptive to the possibility that there is another way, and have a true desire to quit drinking. In the early stages, it is sufficient that the person be receptive to the possibility that there is another way, one that requires a conscious decision to take this alternative path. The first step on this alternative path is the decision to turn one's personal will over to God, as

the individual understands this Higher Power to be. The emphasis on spiritual growth in the AA program rests on the dual assumptions that (a) each person desires a relationship with a Higher Power and (b) it is the individual's distorted perception of the self as the center of the universe that makes him or her vulnerable to alcoholism (McDargh, 2000; Ringwald, 2002).

As part of this ongoing dialogue with the Higher Power, the individual is encouraged to carry out a daily self-examination similar to that of the Examen or Conscience Examen proposed by Ignatius as one of the foundations of the Jesuit order of the Catholic Church. In the Examen, people enter into an ongoing dialogue with their Higher Power while they examine their thoughts, desires, and resentments. It is up to the individual in AA to select his or her Higher Power, and then make a conscious choice to enter into a relationship with that Higher Power. The conscious choice then makes the individual an active participant in the recovery process, as opposed to "patients" who lie passively for treatment to be performed on them (Nowinski, 2003). In this manner, AA offers a program of spiritual growth without a religious dogma, which might offend some members.

One "A" Is for Anonymous

Anonymity is central to the AA program ("Understanding anonymity," 1981), and when honored, it is a major advantage of 12-step groups (Ries, Galanter, & Tonigan, 2008). This is a major reason why most AA meetings are closed. However, in the time since its inception the concept of anonymity has been challenged and sometimes violated in ways that the founders of AA would never have envisioned (Coleman, 2011). Many members have published memoirs in which they identified themselves as members of AA or similar groups, and although the authors only disclose their addiction to alcohol and then their involvement in this self-help group, technically it is still a violation of the admonition of confidentiality (Coleman, 2011). The publication of photographs taken at AA meetings and then posted on the internet is an even more blatant and inclusive violation of the anonymity of the AA meeting.

This trend disturbs many members of the self-help group movement in general, and of AA in specific. Anonymity is a cornerstone of the AA meeting. Who attends AA meetings, what is said at a meeting, and who said it are supposed to remain at the meeting. This presents a dilemma for AA groups that allow people who are court-mandated or employer-mandated to attend. To obtain confirmation that they did indeed attend the meeting, people must ask another

AA member to sign some form of attendance verification, which violates the anonymity of AA meetings. In this manner, the requirements of the court system and those of AA conflict. However, the attendee is still expected to have somebody sign an attendance confirmation form or else face the judge's wrath. The way groups manage this dilemma is up to the individual group—they may decide not to provide the proof of attendance (AA World Services, 2014).

Another aspect of anonymity is that no single person may assume the role of speaking for the entire AA group ("Understanding anonymity," 1981). This allows each member of the group to strive for humility, which is a cornerstone of AA. Each member is equal to the others, and there is no board of directors for the local AA group. Rather, special service boards or committees are set up by the group as the need arises. These boards remain answerable to the group as a whole. The members of the service board or committee are "but trusted servants; they do not govern" (*Twelve Steps and Twelve Traditions*, 1981, p. 10).⁷ Further, because of the equality of members, interpersonal conflict is hopefully avoided or minimized.

Alcoholics Anonymous and Outside Organizations

Each local AA group is both not-for-profit and self-supporting. Each group is autonomous financially, supporting itself only through donations made by members. Further, each member is prohibited from contributing more than \$1,000 per year, and outside donations are discouraged, lest conflict develop within the group as to how the financial windfall should be used. Further, as stated in *Twelve Steps and Twelve Traditions* (1981), AA groups will not "endorse, finance, or lend the AA name to any related facility or outside enterprise, lest problems of money, property and prestige divert us from our primary purpose" (p. 11).

Thus, many AA groups meet in churches, which donate the use of the room(s) for the meeting. Some AA groups, however, do purchase independent buildings in which to hold meetings. These structures are not called Alcoholics Anonymous buildings, as this would violate the sanction outlined earlier. In many cases the structures are called Alono buildings, or by a similar name, but the name Alcoholics Anonymous is not used in the building's name.

⁷The *Twelve Steps and Twelve Traditions* of AA will not be reviewed in this text. Interested readers are invited to read a copy of the "12 by 12," as it is often called. This book can be purchased from the Alcoholics Anonymous World Services, Inc., http://www.aa.org/pages/en_US/twelve-steps-and-twelve-traditions

The Primary Purpose of Alcoholics Anonymous

The AA movement seeks first to provide a program for living to guide the newcomer during the transition stage between active alcohol use and recovery. This is accomplished not by preaching at the member, but by presenting a simple, realistic picture of the disease of alcoholism in the words of other members who have experienced the same (or similar) problems as a result of their own AUD. *Confrontation*, when used, takes a different form than this word normally suggests: In AA, members share their own life stories, making a public confession of sorts in which they give examples of the lies, deceptions, and rationalizations they used to support their own AUD. In so doing, the speakers present a picture of themselves when they were at a stage similar to that of new members, hoping that they will see themselves and the need to join AA now rather than suffer all of the consequences that the speakers outlined in their history.

Service to others is also a central theme in AA, because:

Even the newest of newcomers finds undreamed rewards as he tries to help his brother alcoholic, the one who is even blinder than he. . . . And then he discovers that by divine paradox of this kind of giving that he has found his own reward, whether his brother has yet received anything or not.

Twelve Steps and Twelve Traditions
(1981, p. 109)

In this statement one finds one of the paradoxical components of AA: By helping you, I find part of my own recovery from alcohol. If people were speakers at a meeting, their first step would be an admission that they were powerless over their alcohol use. This is not an admission of helplessness, but only that they were powerless (Wallace, 2003). By joining AA, and with the admission of powerlessness, the members seek the strength of the group as a whole. By admitting the reality of their own AUD, the speaker is reminded of “what my life was like, and by having shared it with you, I am reminded again of the reason why I will not return to drinking again.”

This is the method by which Bill Wilson, in his first meeting with Dr. Robert Smith,⁸ was able to recommit himself to his own recovery. He did not preach but simply spoke about his own history, and then thanked Dr. Smith for listening to his story. In a sense, the speaker asserts that “I am a mirror of yourself, and just as you cannot look into a mirror without seeing your own reflection, so you cannot look at me without seeing a part of yourself.” In so doing, the speaker

benefits as much as the recipient from sharing this message (Zemore, Kaskutas, & Ammon, 2004).

Three factors contribute to the success of AA for a given individual: First is the frequency with which the individual attends meeting. The person who attends a meeting a month will receive less benefit from the group process than the person who attends two meetings a week, for example. Second is the individual's level of participation in the meeting. The individual who sits quietly in the back of the hall and then slips quietly away at the end of the meeting will derive less benefit than the person who actively participates in meetings, asks questions, meets with members after the meeting to discuss points that they are confused about, and so on. This active AA involvement appears to reflect some of the forces that predict successful efforts to change (Moos & Moos, 2005; Nace, 2003). Finally, there is the emphasis not on long-term recovery, but on simply keeping the focus on “one day at a time,” which is the third factor that appears to predict success. Individual members are encouraged not to worry about distant problems, but to keep the focus on the problems that might undermine their recovery program today. They will have time to worry about tomorrow's problems when tomorrow arrives, or so it is believed.

Outcome Studies: The Effectiveness of Alcoholics Anonymous

Since its inception in the mid-1930s, virtually every element of AA has been questioned, challenged, and defended. Still, in spite of almost a century of experience and research into the issue, the question remains: Is AA effective? Many professionals view AA as being the single most important element of an individual's recovery program. However, AA is not a single entity, and the format of meetings varies from one AA group to the next (Arkowitz & Lilienfeld, 2011). Thus, we are left with the conundrum of referring individuals to a support system that is not definitely shown as effective, and that would be quite challenging to show as effective. Of course, one must also consider previous meta-analytic data that indicates that “although there is no conclusive evidence to show that AA can help to achieve abstinence, nor is there any conclusive evidence to show that it cannot” (Ferri, Amato, & Davoli, 2006, p. 11).

In spite of clinical lore, there has been relatively little research into (a) whether people referred to AA actually attend group meetings, (b) the degree of their involvement or participation in these meetings, and (c) the effectiveness of the 12-step group (Ferri et al., 2006). One study that did attempt to address some of this lack of research on AA was conducted by Kaskutas and colleagues (2005). This study

⁸Often referred to as “Dr. Bob” in the AA group movement.

examined the post-treatment AA participation of 349 people who had entered a formal treatment program for an AUD. The authors found that the post-treatment AA involvement of their research subjects fell into four subgroups:

- *Low AA involvement:* These people attended AA just during the first year following treatment.
- *Medium AA involvement:* Individuals in this subgroup attended about 60 AA meetings in the first year following discharge from treatment, but had slightly increased their level of AA involvement by the fifth year following discharge.
- *High initial AA involvement:* Individuals in this subgroup attended 200 meetings in the first year following discharge from treatment, with a slight decrease in their level of AA involvement by the end of their fifth year following discharge.
- *Declining AA involvement:* Individuals in this subgroup initially attended 200+ AA meetings in the first year following discharge from treatment, but by the end of the fifth year following discharge this had fallen to about six meetings a year.

Further, Kaskutas and colleagues (2005) found that there was a correlation between abstinence and level of AA group involvement, with 79% of those people in group 1 were abstinent⁹ from alcohol, and 73% of those people whose level of AA group involvement placed them in group 2 were still abstinent from alcohol at the end of the fifth year. Sixty-one percent of those individuals who fell into group 3 were still abstinent from alcohol at the end of the fifth year, whereas 43% of those individuals in group 4 were still abstinent at the time of the follow-up study. Frings, Collins, Long, Pinto, and Alberly's (2016) research found that those who attended recovery meetings and identified highly with the group were more likely to see relapse as costly to them and the other group members, and saw the social control of the group as a positive for their recovery. Additional research, with statistical methods that are said to remove the so-called **self-selection bias** (defined as individuals who are in a given group self-select to be there, and thus are more ready to change), has found that increased AA attendance does lead to short- and long-term gains in relation to alcohol consumption, particularly for those who do not already have high involvement (Humphreys, Blodgett, & Wagner, 2014). Interestingly, Zemore, Kaskutas, Mericle, and Hemberg (2017) found that those who attend non-12-step abstinence-based groups (such as those discussed later in this chapter) may attend less frequently

than those who attend AA, but have higher satisfaction and sense of community.

Brust (2007a) suggested that AA had a success rate of 34%, but did not elaborate as to the criteria utilized to reach this conclusion. Lemonick and Park (2007) suggested that AA was effective "about 20% of the time" (p. 42). Other writers indicate that of those who attend AA or other 12-step groups regularly after outpatient treatment, only about 22–25% are *not* clean/sober between 1½ and 2 years later (Emrick & Beresford, 2016). Although the research on AA continues to be debated, current research does suggest that, although AA and other 12-step programs are not for everyone, there is sufficient evidence to include them for consideration for treatment recommendations, though not to require them of everyone (Mendola & Gibson, 2016).

There is a growing body of evidence suggesting that 12-step-oriented treatment programs have higher success rates and lower costs than programs without such a focus (Humphreys & Moos, 2007; Ries et al., 2015). Humphreys and Moos (2007) found that treatment programs that included 12-step group involvement were 30% less expensive than cognitive-behavioral programs and that 30% more clients from the 12-step involvement group were alcohol-free at the end of 2 years. These findings suggest that 12-step programs can serve an important adjunctive role in substance rehabilitation programs.

Data obtained from national surveys¹⁰ have found that the average AA member has almost 10 months of sobriety, that 49% have been alcohol-free for more than 60 months, and that 27% have less than 12 months of recovery to their credit (AA World Services, 2014). Individuals who have been found to be less active in group meetings appear to be most likely to relapse (Chappel & DuPont, 1999; Gitlow, 2007; Zemore et al., 2004). Unfortunately, there is no objective way to measure participation. A given person might claim to have attended several 12-step group meetings recently, but he or she might have sat in the back of the room, arrived late, left early, never spoken with anyone, and didn't have a sponsor (Gitlow, 2007, pp. 226–227).

The need for the individual to be actively involved in a 12-step group makes sense, because programs such as AA offer such things as (a) external supervision, (b) substitute dependency, (c) new abstinence-centered supportive relationships in place of alcohol-centered relationships, and (d) increased spirituality (Kelly & Yeterian, 2011; Vaillant, 2000, 2005). Having a sponsor, especially during the first year of the recovery effort, appears to be a helpful addition to the

⁹Which the authors of this study defined as no alcohol use in the past 30 days.

¹⁰One problem with surveys is that those people who choose to participate in the study are, by definition, different from those who decline to do so.

individual's AA program (Tonigan & Rice, 2010). Further, involvement in the process of helping newcomers to AA also appears to assist the helper in their struggle to maintain abstinence, an observation that reinforces the need for active participation in the AA program to assist the individuals in their recovery (Pagano, Friend, Tonigan, & Stout, 2004).

Although many 12-step–based rehabilitation programs require 12-step group involvement while the person is in treatment, AA group involvement after discharge from treatment is positively correlated with sobriety (Arkowitz & Lilienfeld, 2011; Brigham, 2003; Moos & Moos, 2005, 2006a; Nace, 2003). Moos and Moos (2006a) found, for example, that individuals who remained active in AA following discharge from treatment had better outcomes than did those people who did not, and that people who participated in AA by attending at least 27 meetings in the first year following discharge were more likely to be abstinent both in the second year following discharge and again 16 years later. Thus, involvement in AA appears to mirror the individual's efforts to make meaningful changes in other areas of his or her life, such as developing nonchemical means to cope with stress.

Unfortunately, the very nature of AA and similar self-help groups makes it virtually impossible to design a study that would isolate those elements that might help make AA effective, and the patient characteristics of those who are most likely to benefit from a 12-step group such as AA (Gernstein, 2003). By definition, people who join AA are not representative of those people who have an AUD, if only because of their decision to join AA.¹¹ Those people who drop out of AA are, by the very fact that they dropped out of this self-help group movement, different from those who remain active in it. Given the fact that at the end of 3 months at least half of the new members who joined will have dropped out, and that at the end of 1 year 95% of new members will have stopped attending meetings (Nace, 2003), it must be asked how representative those who remain in this self-help group program are of those with AUDs.

Although these studies are suggestive, there is still insufficient evidence at this time to answer the question whether AA is effective in the treatment of AUDs. One point of continuous confusion is the AA program's emphasis on spirituality, as opposed to religion. The available evidence does not suggest that the individual member's religious beliefs change while they participate in AA, although they do grow spiritually (Robinson et al., 2007). This spiritual growth is then associated with a higher abstinence rate (Kelly, Stout, Magill, Tonigan, & Pagano, 2010; Robinson et al., 2007). It is assumed that spirituality-based recovery programs might be

most effective for those people who had strong religious beliefs prior to the onset of their AUD (Cooney, Kadden, & Steinberg, 2005); however, this is only a theory.

Narcotics Anonymous¹²

In 1953, a new self-help group that followed the AA model was founded, calling itself Narcotics Anonymous (NA). Although this group honors its debt to AA, the members believed that:

We follow the same path with only a single exception. Our identification as addicts is all inclusive in respect to any mood-changing, mind-altering substance. "Alcoholism" is too limited a term for us; our problem is not a specific substance, it is a disease called "addiction."

Narcotics Anonymous (1982, p. x)

To the members of NA, the problem was the common disease of addiction. This self-help group emerged for those whose only "common denominator is that we failed to come to terms with our addiction" (*Narcotics Anonymous*, 1982, p. x). Many outsiders view the major difference between AA and NA as being one of emphasis: AA addresses only AUDs, whereas NA addresses addiction to chemicals including alcohol. Indeed, whereas in the first step of the AA's 12-step program the word "alcohol" is used, the first step of the NA program uses the word "addiction."

The growth of NA has been exceptional. Currently, there close to 67,000 weekly meetings in 139 countries (*Narcotics Anonymous*, 2016). Each self-help group offers a similar 12-step program offering the person with an addiction a day-by-day program for recovery. This is not surprising, because NA members based their program on AA. Some people are quite comfortable going to AA and believe that this group offers them all that they need to address their SUD. Others believe that NA is a better group for them because it addresses substance use disorders other than just alcoholism. There appears to be no inherent advantage of one program over the other. It is more important to determine which group works best for which individual.

Other 12-Step Groups

Many additional 12-step groups have developed over the years, as individuals have desired meetings specific to the

¹¹Yet it was on a sample drawn from members of AA that Jellinek (1960) based his research on alcoholism, raising questions about the validity of his research.

¹²Alcoholics Anonymous and Narcotics Anonymous are not affiliated with each other, though there is an element of cooperation between the two organizations (M. Jordan, personal communication, February 27, 1989).

drug of misuse. For example, Cocaine Anonymous (CA) was formed in 1982 (Chaney, 2016), and Nicotine Anonymous (NicA) also began in the early 1980s (*Welcome to Nicotine Anonymous*, 2015). Crystal Meth Anonymous (CMA) was founded in 1994 (*CMA History of Service*, 2017). Heroin Anonymous (HA) began in 2004 (*History of Heroin Anonymous*, 2016), whereas Opiates Anonymous (OA) began in 2013 (*Welcome to Opiates Anonymous World Services*, n.d.). It certainly behooves the professional to have a full sense of the availability of groups in the area where a client lives before automatically assuming that AA is the only option.

Al-Anon

The book *Al-Anon's Twelve Steps and Twelve Traditions* provides a short history of this movement. In brief, while those with AUDs were attending one of the early AA meetings, their partners would meet to talk about various topics, including their significant others. At some point the decision was made to adapt the same 12 steps that their partners found so helpful in their own recovery program, and the Al-Anon movement was born. At the start of the 21st century there were an estimated 30,000 Al-Anon groups in the United States, with an estimated 390,000 members (Gwinnell & Adamec, 2006; White, 2005).

Although at first each group modified the 12 steps as they felt necessary, by 1948 the wife on one of the cofounders of AA became involved in the growing organization, and over time a uniform support group for family members of AA members emerged. This was a self-help group movement that was organized in response to the fact that 86% of members of families in which there was an alcohol-dependent person felt that their mental health had suffered as a result of the AUD of the other person (Gwinnell & Adamec, 2006). The program that evolved from this phenomenon was known as the Al-Anon Family Support Group, which made minor modifications to the *Twelve Steps and Twelve Traditions* of AA to make them applicable to the needs of family members.

Surprisingly, family members find it useful to attend Al-Anon meetings even if the family member using substances continues to misuse chemicals. This not only allows family members to learn how to deal with the stress of a substance-abusing member, but in approximately 20% of cases the individual misusing substances eventually agrees to enter a treatment program (O'Farrell & Fals-Stewart, 2008).

Alateen

By 1957, it was recognized that teenagers presented special needs and concerns, and the Al-Anon program was modified

to provide a group for these individuals, a group that came to be called Alateen. There are more than 2,300 Alateen groups in the United States (Capretto, 2007; Gwinnell & Adamec, 2006), as well as chat sessions available through the website (<https://al-anon.org/al-anon-meetings/virtual-meetings>). Alateen programs follow the same 12-step program outlined in the Al-Anon program, but provide an opportunity for teenagers to come together to share their experiences and problems, and to provide encouragement to each other. The group also provides information about the disease of alcoholism, how these teens did not “cause” the alcoholism in their families, how to detach from the alcoholism in their families, and how they can build a rewarding life in spite of the continued AUD in their family.

Support Groups Other Than 12-Step Groups

There has been a great deal of criticism aimed at 12-step groups such as AA and NA because of their emphasis on spirituality or their failure to empower women, for example. In response to this criticism, several other support groups have emerged, some of which will be discussed next.

Rational Recovery¹³

The Rational Recovery (RR) movement attempted to apply the tenets of cognitive-behavioral psychology to the problem of substance use disorders. This movement discontinued group meetings in January 2000 (Horvath, 2011). In place of group meetings, RR utilizes services available through books, videos, and internet-based material designed to help the individual recognize, and then change, “addictive thoughts” that contribute to the individual's continued use of chemicals. This program uses a different methodology than does AA, and suggests that the “one-day-at-a-time” philosophy of AA is counterproductive rather than supportive of a recovery program (Rational Recovery Systems, Inc., 2008).

Self-Management and Recovery Training (SMART)¹⁴

This program was started in 1985, and has meetings in the United States, the United Kingdom, and Australia, with online meeting options as well. SMART was originally part of the Rational Recovery movement, but broke away from

¹³www.rational.org.

¹⁴www.smartrecovery.org.

it in 1994 (Horvath, 2011). The SMART program draws heavily on cognitive-behavioral schools of therapy, and has four central goals for adults with SUDs: (a) to enhance and maintain the individual's attempt to abstain from alcohol or drugs, (b) to help the individual learn how to cope with thoughts or cravings about chemicals, (c) to help the individual resolve old conflicts and problem behaviors, and (d) to develop a lifestyle balance (Gernstein, 2003; Horvath, 2000). The SMART program maintains that the individual's misuse of alcohol or other chemicals is the result of self-defeating thoughts such as "I have a right to use [X]!" or that their misuse of chemicals is not really the cause of all their problems. Yet another category of dysfunctional thoughts are those that allow the individuals to rationalize their relapse back to active substance use ("You made me so angry that I went out and drank!").

SMART groups believe that virtually any approach to recovery will be of some value to the individual and thus encourages participation in traditional 12-step groups (Horvath, 2000). About 10% of SMART group members also participate in AA groups (Gernstein, 2003). Participants are taught how to view abstinence as a form of self-affirmation and how not to rely on substance use for good feelings about themselves.

Secular Organizations for Sobriety (SOS)¹⁵

This self-help group was founded in 1985 by James Christopher, and by 2000 it was estimated that there were more than 2,000 SOS groups in existence, although the program has been viewed as struggling by some (Gernstein, 2003). They also have online groups available for support. SOS groups are a response to what is perceived as a heavy emphasis on spirituality in traditional 12-step groups (Ringwald, 2002). The guiding philosophy is heavily influenced by the cognitive-behavioral psychotherapy principles, and stresses personal responsibility, the role of critical thinking in recovery, and the identification of each individual's "cycle of addiction" (Horvath, 2005).

The SOS model postulates that the addictions rest on three elements: (a) the physiological need for the chemical brought about by tolerance, (b) the learned habit of using chemicals as a way to cope, and (c) the denial of (a) and (b) (Horvath, 2005). In contrast to traditional 12-step groups that suggest that the individual must rely on a Higher Power to abstain, SOS holds that the individual has the potential within himself or herself to learn how to live without chemicals (Ringwald, 2002). The program takes a neutral stance toward participation in traditional 12-step groups, and a

significant portion of members are either currently attending a 12-step group or have done so in the past.

Women for Sobriety (WFS)¹⁶

This self-help group movement was started in 1976 by Jean Kirkpatrick, who passed away in June 2000 at the age of 77 (Horvath, 2000). This organization is specifically for women, in response to the belief that traditional 12-step groups have failed to address how recovery from the addictions requires different forms of support for men as opposed to women. There are 13 core statements or beliefs in WFS, which are designed to assist the member in building self-esteem and a new perspective of the self that is not based on the use of chemicals. Unlike more traditional 12-step groups, WFS members are encouraged to leave the group when they feel that they are ready to graduate from the program and assume responsibility for their own recovery (Ringwald, 2002). Thus, the small number of active members actually does an injustice to the program, because only a fraction of the members are actively involved in the program at any one time. It continues to grow, despite the death of the founder, with an updated mission statement for the new century approved in 2011 (Fenner & Gifford, 2012).

Moderation Management (MM)¹⁷

Moderation Management was founded in the early 1990s and has been quite controversial since its inception. The founder, Shirley Kishline, was frustrated with traditional 12-step group programs. She had been referred to 12-step-based treatment programs over the years, but her own addiction to alcohol was never firmly established in her mind, and she believed that she was only a "problem drinker" (Kishline, 1996, p. 53). Kishline defined a problem drinker as a person who consumed only 35 drinks per week and who had experienced only mild to moderate alcohol-related problems. The MM core philosophy rests on the foundation that nine out of ten problem drinkers avoid more traditional 12-step groups and that they shun the traditional label of "alcoholic" (Horvath, 2005; Humphreys, 2003; "What is Moderation Management?," 2008). The alcohol-dependent person, in contrast, is the person who would experience severe withdrawal symptoms if he or she should discontinue the use of alcohol, in Ms. Kishline's opinion.

Moderation Management maintains that moderation should be a more appropriate goal than abstinence for many people, especially those who are not physically dependent on alcohol (Kelly & Yeterian, 2011). Members of MM were

¹⁵<http://www.sossobriety.org/>.

¹⁶www.womenforsobriety.org.

¹⁷www.moderation.org.

encouraged to work on the goal of consuming no more than four standard drinks in any given 24-hour period (Horvath, 2005). Initially, the MM concept gained support, and MM groups were established in approximately 25 states. Then the founder, Ms. Kishline, was involved in an alcohol-related motor vehicle accident in which her vehicle struck another on an interstate highway, killing a man and his son. Her measured blood alcohol level was 0.260, or more than three times the level defined as legal intoxication in that state, resulting in legal charges and a conviction (Noxon, 2003). It is not clear how the arrest of the founder of Moderation Management, her subsequent death in late 2014, or its low measured success rate¹⁸ will affect the MM movement. This is unfortunate because the teachings of MM are not totally contrary to those of more traditional 12-step groups, and many individuals were members of both groups. As of 2017, they list 34 meeting locations in seven countries (the majority of meetings being in the United States), with eight additional emerging meetings, as well as online options for support (www.moderation.com). Some research has supported the idea that those who are not physically dependent can reduce their drinking to an appropriate level with proper support (Hester, Delaney, & Campbell, 2011). Research has found that at best only about 18% of people once dependent on alcohol can learn to drink in moderation again (Lilienfeld, Lunn, Ruscio, & Beyerstein, 2010), a finding that raises questions about the legitimacy of the theory on which MM was based.

LifeRing¹⁹

This is another abstinence-based alternative to traditional 12-step groups. Started in 1999, it is based in California and did not become national until 2001 (*Discover LifeRing*, n.d.). LifeRing rejects more traditional 12-step groups, in part because of what it views as the inflexible nature of such groups. LifeRing maintains that there are multiple paths to recovery, as opposed to the single path suggested by traditional 12-step groups. Further, LifeRing maintains that the individual's spirituality is a private matter. However, members are not discouraged from attending more traditional 12-step groups, either.

Each individual is encouraged to develop a recovery program that will fit her or his needs, guided by the central philosophy of "whatever works" for that person. Currently there are meetings in about 16 states and four foreign countries, as well as online meetings. Members tend to be white, middle-aged, college-educated individuals, with a slight

preponderance of male members (58%) over female members (42%) (White & Nicolaus, 2005). Research is under way to compare the effectiveness of this relatively new recovery program with other groups, such as AA and SMART Recovery (Zemore, 2016).

Faith-Based Recovery Initiatives

There is a growing trend for recovery programs to be established to function within the religious doctrines of different churches or religious backgrounds. Such programs range from well-established to fledgling programs, and there are too many to be discussed here. Although there are many different and developing groups, examples include Celebrate Recovery (<http://www.celebraterecovery.com/>), Alcoholics Victorious (<https://alcoholicsvictorious.org/>), Buddhist Recovery Network (<http://www.buddhistrecovery.org/>), and Jewish Alcoholics, Chemically Dependent Persons and Significant Others (JACS; <https://jewishboard.org/listing/jewish-alcoholics-chemically-dependent-persons-and-significant-others-jacs/>).

Minority Group–Oriented Recovery Programs

There are a small number of programs that attempt to address the particular needs of members of a minority group who have a substance use disorder. Such programs tend to be local initiatives serving the needs of minority group members in a limited geographic area. One good example is the Healing Journey program at the Minnesota Indian Women's Resource Center (Fletcher, 2013). Such programs attempt to integrate the traditional beliefs of a specific minority group with more traditional recovery-oriented self-help groups such as AA.

Challenges to the Traditional 12-Step Movement

The traditional 12-step movement has established an almost irreproachable status in the addictions recovery community, and clinical researchers who suggest that total abstinence from alcohol or illicit drugs might not be the best goal are often accused of committing what might be called "medical blasphemy" (Lilienfeld et al., 2010, p. 234). However, in spite of the privileged status that traditional 12-step groups hold within society, they are not without a small, vocal group of critics. In this section, we will review some of the criticism of the AA program, which, as the earliest program to be established, has drawn the greatest level of criticism. However,

¹⁸In response to those critics who will scream that 18% is a significant success rate, would you want to undergo a surgical procedure that had an 82% failure rate (possibly leaving the patient with no benefit, possible significant medical sequelae, or even death)?

¹⁹www.lifering.org.

each point discussed next could also be applied to the other 12-step group movements discussed earlier.

A charge often made by those who do not wish to attend meetings is that the traditional 12-step groups are “cults.” This charge is inaccurate because, unlike cults, which have a defined hierarchy or leader(s), AA does not (Newsome, 2011). Additionally, AA does not prevent people from leaving the “fellowship,” nor is the aim to control people (Wiechelt, 2015). In spite of this, the charge has been made that public confession of past transgressions by members and testimonial speeches by those who attribute their recovery to a 12-step group appear “more like a Baptist tent revival than a recovery program”²⁰ (Newsome, 2011, p. 125). Further, it is often pointed out in traditional 12-step group meetings that whereas people might be recovering from an SUD, they have never fully recovered or been cured (Fletcher, 2003; Gilliam, 1998). They remain dependent on the group for continued assistance and support for the rest of their lives, with over 20% of members having been sober for more than 20 years, with the average length of sobriety at half that (AA World Services, 2014). Yet the AA “Big Book” repeatedly speaks of people having “recovered” from alcohol dependency and as no longer needing to attend meetings to maintain sobriety (Fletcher, 2003). This fact, critics of the movement often point out, is quietly ignored by proponents of 12-step programs.

A major criticism of traditional 12-step groups is that they are based on a fundamentalist tradition of the 1840s known as the Washington Revival (Newsome, 2011; White & Nicolaus, 2005). This was essentially a white, conservative Protestant movement that replaced physicians and ministers who were providing temperance lectures with laypeople who were “reformed” or “reforming” (White & Nicolaus, 2005, p. 58). The influence of this movement on the early AA movement might be seen in the emphasis on public confession of one’s addiction to alcohol (White & Nicolaus, 2005). The leaders of the Washington Revival were later charged with “the sin of humanism” (White & Nicolaus, 2005, p. 59), which is to say, placing their own will above that of God, and were subsequently discredited by the religious authorities of the time. However, the lessons of attempting to establish a secular recovery group were remembered, and eventually these lessons helped to form the foundation of the Oxford Group, which immediately preceded the formation of AA.

These lessons were heeded by the founders of AA, who attempted to strike a middle ground between the secularity of the Washington Revival and the religious orientation of the Oxford Group. However, courts in the United States have ruled that AA cannot be required without offering

secular options as well (Wiechelt, 2015). These rulings are based in part on the program’s heavy emphasis on an external, possibly supernatural, Higher Power that the individual must “surrender” to as part of her or his recovery program (Gernstein, 2003; Wallace, 2003; Wiechelt, 2015). The courts have repeatedly ruled in various states that forcing an individual to attend such a group violates the law (Peele, 2004b). This has not prevented other local courts from offering persons with an AUD the choice of attending AA as an alternative to incarceration, as technically the individual “chooses” to attend the 12-step group meetings and is not being forced to do so.

When the program is forced upon the individual (by the courts, family members, etc.), or if the group is very confrontational, the potential exists that it can be more harmful than helpful (Arkowitz & Lilienfeld, 2011; Szalavitz, 2006). This may be one reason why only 33% (Lillienfeld et al., 2010) to 50% (Nace, 2005a) of new members remain active in AA by 3 months after their initial meeting. To further complicate matters, there is past research that found people who are court-mandated to attend AA following an arrest for driving a motor vehicle while intoxicated have a higher recidivism rate and worse subsequent driving records (as evidenced by motor vehicle accidents, for example) than those people sentenced to incarceration by the courts (Bufe, 1998).

Another challenge to the 12-step group movement is based on the fact that there were only a limited number of people (100 individuals) who had achieved abstinence when the 12 steps were formulated. The worldview of these early members was formed during the Great Depression of the 1930s and was designed to deflate the individual’s ego during a time when many struggled to maintain self-esteem.²¹ This is justified on the unproven assumption that grandiosity is a common characteristic of alcohol-dependent people. This core assumption can be disempowering to individuals who join a 12-step group (Newsome, 2011), and the applicability of these assumptions to a person living in the 21st century has been questioned. “A vibrant society,” Frances (2013) noted, “depends on having responsible citizens who feel in control of their actions and own up to the consequences of their actions” (p. 191). This perspective is often seen as diametrically opposed to the tenets of the 12-step movements.

Further, the AA program has been seen as a one-size-fits-all program, which demands conformity to a single approach to recovery and discourages individuality (Newsome, 2011). It has even been charged that 12-step groups follow

²⁰With apologies to readers who are Baptist.

²¹The unemployment rate was estimated to reach 25% or higher during the height of the Great Depression.

a process of “indoctrination” (Bufo, 1998, p. 6) and fear. The individual is repeatedly warned that the disease of alcoholism will automatically progress, and that the individual must rely on the strength of the group to overcome individual weakness and avoid a relapse. These assertions that are not supported by the clinical research²² that suggests that those with AUDs rarely follow the downward spiral thought to be inescapable by AA, but alternate between periods of more and less abusive drinking (Vaillant, 2000). Further, the 12-step program does not attempt to address the issue that AUDs can take many forms and that there is no single road to alcoholism. Rather, the individual is offered a single program as a road to recovery. Indeed, Szalavitz (2006) took this criticism even further, noting that the 12-step program has been adopted virtually unchanged to address a wide range of maladaptive behaviors such as overeating, heroin addiction, compulsive shopping, and so on. Not only is it a one-size-fits-all program, but a “one treatment model fits all problems” approach as well!

It is a common belief that the spiritual experience of one of the original founders of AA, Bill Wilson, was a critical step in the evolution of the AA movement. A little-known fact, however, is that this experience was possibly aided by a belladonna injection²³ administered by his physician to help him overcome the acute effects of alcohol withdrawal²⁴ (Bufo, 1998). Thus, the foundation stones on which AA was based may have at the very least been a medication side effect, if not the result of the combined effects of the alcohol withdrawal process and the belladonna. Another criticism of the 12-step program is the emphasis on waiting until the individual “hits bottom” and reaches a state of spiritual desperation. In any other field of psychological or psychiatric treatment, waiting for the individual to hit bottom would be branded abusive by the mental health community (Fletcher, 2003). Although this belief is growing less and less common in AA, there are still those who espouse it as necessary for the alcoholic to reach this step before attempting to intervene.

Other critics of the 12-step group movement point out that it is based not on a foundation of scientific research, but on testimonials by individuals who assert that it was indeed essential to their recovery. Anecdotal stories, though perhaps

very moving, do not constitute scientific research data supporting claims that AA or similar groups are effective. However, just as individuals who were “recovered” or “recovering” replaced physicians or ministers as speakers at temperance meetings, in many 12-step meetings one person is a designated speaker who affirms how the group saved his or her life. Dissenting opinions from mental health professionals are often dismissed because they “do not understand” the disease of addiction, or because they have “not been there.”²⁵ In contrast, program participants are elevated to the role of “experts” because they were once actively addicted to chemicals (Szalavitz, 2006).

Finally, research has demonstrated that only about 20% of those who join AA will abstain from alcohol for the rest of their lives (Lilienfeld et al., 2010), although this statistic and other similar statistics certainly have been called into question (Emrick & Beresford, 2016), one concern being whether abstinence for lifetime is truly the goal. For years, AA was the only option for many, and after treatment programs surfaced, the only aftercare option out there; however, there are now many other options other than AA and similar 12-step groups (Wiechelt, 2015). As these various points of criticism suggest, although the 12-step group movement may have played a major role in recovery, there are many points of contention suggesting that these programs are not a panacea for individuals with alcohol (or, by extension, other drug) use disorders.

Chapter Summary

Alcoholics Anonymous was one of the first, and has grown into the predominant self-help group model for individuals with an AUD. The program emerged as the first members of the fledgling AA group movement who achieved long-term abstinence met to discuss the common elements that contributed to their recovery. This consensus resulted in the famous 12 steps of the AA program.

The AA program is designed to place emphasis on spiritual growth, without addressing religious issues. It is confrontational without using confrontation, relies on external support for advertising or financial resources, and is not required of members but simply offered as a road that members might find useful in their quest for recovery from alcoholism. There is no board of directors, and members who serve in various capacities do so as an equal among equals.

²²This clinical research, however, is ignored on the grounds that researchers just do not understand the disease of addiction, as will be discussed later in this chapter.

²³This was an acceptable treatment method for alcohol withdrawal symptoms at the time.

²⁴Another obscure fact is that Bill Wilson advocated the use of LSD to help the individual overcome some of the obstacles that prevented the person from achieving lasting recovery (Newsome, 2011).

²⁵So when you are having a heart attack, will you demand that you be cared for only by a physician who has “been there” by having a prior heart attack?

The growth of AA was slow initially, but it has become a worldwide movement, with chapters in virtually every nation around the world, and has a total membership in the millions.

Questions have been raised about the effectiveness of AA as an adjunct to treatment for people with an AUD. By extension, these same questions apply to self-help groups modeled after the AA program. There is preliminary evidence suggesting that AA is a useful adjunct to the treatment of some, but not all, people with an AUD. Variations of the program have been applied to other problems, such as being

the spouse of a person with an AUD (Al-Anon), and being the child of a person with an AUD (Alateen).

The AA program was also modified and applied to other drugs, resulting in programs such as Narcotics Anonymous, which was reviewed in this chapter. It has also been applied to a variety of non-drug-related compulsive behaviors such as compulsive eating, compulsive shopping, and so on. Further, there are a number of newer self-help programs that reject one or more of the tenets of the AA program, but that still attempt to help individuals find abstinence from alcohol and other drugs.



CHAPTER 36

Substance Use Disorders and Infectious Disease¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 36.1** Understand why infectious disease is a concern for those with SUDs
 - 36.2** Identify the bacterial infections that may be encountered in those who use intravenous drugs
 - 36.3** Review the pneumonias that may be seen in those with SUDs
 - 36.4** Review the concerns with tuberculosis in those with SUDs
 - 36.5** Review the history related to HIV and the impact in relation to SUDs
 - 36.6** Identify the hepatitis infections that may be encountered in those with SUDs
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Introduction

As a group, those who use alcohol and illicit drugs are approximately twice as likely as nonusers to use the services of a hospital emergency room, and seven times as likely to require hospitalization (Laine, et al., 2001). In 2011, the last year that the Drug Abuse Warning Network (DAWN) gathered data, over 5 million emergency room visits were drug-related, which was up almost 30% from 2009, and up 100% from 2004 (SAMHSA, 2013). Once admitted, individuals with a substance use disorder (SUD) tend to require longer hospital stays before being ready for discharge. The increased risk for infectious disease found in people with SUDs is one reason for these expensive extended hospital stays.

The SUDs contribute to infectious disease(s) through a variety of mechanisms. Chronic alcohol use depletes the body of essential nutrients, reducing the effectiveness of the immune system, while aspiration of regurgitated material can contribute to pneumonia. Intravenous drug use, unless carried out under antiseptic conditions, pushes bacteria normally found on the skin into the circulation, bypassing the body's normal defenses against such invasion. Sharing compounds for smoking (such as marijuana, for example) allows infectious microorganisms in the lungs to be passed from one

¹The author would like to express his appreciation to John P. Doweiko, MD, for his previous reviews of this chapter for technical accuracy.

person to the next. The general environment in which those who use illicit drugs live also predisposes them to infections. Some of the infectious diseases more commonly encountered in those who use illicit drugs include peripheral cellulitis, skin abscesses, pneumonias, lung abscesses, brain abscesses, various viral diseases, and tetanus. In this chapter, we will discuss some of the more common infections associated with the SUDs.

Why Is Infectious Disease Such a Common Complication for People with an SUD?

There are many answers to this question. The general state of malnutrition so often found in the person with an SUD can compromise the effectiveness of the body's immune system. The individual struggling with a methamphetamine addiction might subsist on a "diet" of soda and candy bars, for example. Those individuals with an AUD might, if asked, assert that they did indeed have dinner last night. When the matter is pursued, the drinker might admit that he or she had two bags of peanuts, some pretzels from the bowl on the bar, and half a hamburger, along with almost a dozen bottles of beer, a diet that is hardly going to support a healthy immune system and which might be exacerbated by alcohol-induced damage to the immune system.

Sterile Technique

The conditions under which those who use illicit drugs inject their drug(s) of choice make some form of infection almost certain. This is because the individual injecting drugs rarely uses the sterile technique used by health care professionals. If a compound must be injected into the body, health care professionals will use a new, sterile needle, and prepare the injection site with either alcohol or an antiseptic solution before injecting a sterile compound into the patient's body. The needle is then safely discarded. In contrast to this process, many of those who use intravenous drugs usually just find a vein and insert the needle without even attempting to wash the injection site with soap and water. In the process, microorganisms found on the surface of the skin are pushed into the body, effectively bypassing the body's normal defenses.

Contamination

Illicit drugs are often contaminated with various microscopic pathogens, which are then injected directly into the body if the drug is administered via intravenous injection. Surprisingly,

although pharmaceutical preparations are highly prized among those using illicit drugs because of their purity and known potency, they also might become contaminated as the individual prepares the capsule or tablet for injection. The tablet or contents of the capsule are crushed into a fine powder so that it might be prepared for injection. The flat surface that is selected for this process, however, might be contaminated, transferring microorganisms to the compound about to be injected. If they are sharing a needle, some individuals using intravenous drugs do not even attempt to sterilize it. At best, they might lick the needle to clear off residual blood, and in the process transfer bacteria such as *Nisseria sica* and *Streptococcus viridans* to the needle surface. These are bacteria normally found in the human mouth, where the body has developed defenses against them, but by injecting them directly into the body, these defenses are avoided.

Some users of intravenous drugs do attempt to rinse the *rig* (slang term used to refer to the needle) in tap water. This process contaminates the needle with various microorganisms normally found in tap water (which when swallowed are destroyed by the body's defenses). These microorganisms are then injected directly into protein-rich muscle tissue or the general circulation, depending on the method by which the compound is misused, again sidestepping the body's natural defenses against such microscopic invaders. The stage is now set for either a localized or a systemic infection.

The list of infectious diseases that might be transferred from one individual who uses IV drugs to the next through contaminated needles includes (but is not limited to) the various viral forms of hepatitis, HIV-1 (the virus that causes AIDS), syphilis, and even malaria. Some of the more commonly encountered infections seen in those who misuse substances are discussed in this chapter.

Assorted Bacterial Infections Seen in Individuals Using Intravenous Drugs

Infective Endocarditis

Infective endocarditis (IE) is a bacterial infection of the valves of the heart (although the endocardial surface can be infected as well, as can cardiac devices; Cahill & Prendergast, 2016). There has been an increase in the prevalence of IE in the United States, with current estimates that 15 individuals out of 100,000 are infected (Pant et al., 2015). Those who use intravenous drugs are considered a high-risk population, with 1 in every 500 users of intravenous drugs developing this disorder (Robinson, Lazo, Davis, & Kufera, 2000). Interestingly, although 10% of IE cases

occur in those who use intravenous drugs, when the IE infects the right side of the heart, the majority of the patients are those who use intravenous drugs (Colville, Sharma, & Albouaini, 2016). One reason for IE in those using drugs is the chronic exposure to the irritating chemicals often used as adulterants. But another cause is the failure of those who use intravenous drugs to follow sterile technique: Many of the strains of bacteria that are introduced into the body colonize the tissues of the heart valves upon reaching them, establishing ongoing endocarditis. Finally, shared needles may transfer bacteria from one person with endocarditis to another individual, who then goes on to become infected in turn.

Skin Abscesses

The individual who uses drugs intravenously or subcutaneously is vulnerable to bacterial infections at the injection site. A commonly known risk factor is the use of *speedballs* (cocaine and heroin) (Creamer & Gossop, 2016). Some of the adulterants mixed with heroin or cocaine will either cause or exacerbate skin abscesses. These adulterants are usually not water-soluble, irritating surrounding tissues, and since the injection site is rarely washed with an antiseptic solution, bacteria normally found on the skin are pushed into the blood-rich tissues under the skin when a compound is injected. These abscesses may become life-threatening, require prolonged treatment, and leave the individual with scars at the infection site for the rest of their lives . . . if they survive. Such infections are often lethal for the individual using intravenous drugs.

Necrotizing Fasciitis

This is a specific form of skin abscess in which subcutaneous tissues are attacked by strains of bacteria normally found only on the surface of the skin (Karch, 2009). Those who use cocaine might be especially vulnerable to this condition, possibly because of the vasoconstrictive effects of this compound. However, any user of intravenous drugs who fails to utilize proper sterile technique will push any bacteria at the injection site through the skin into the subcutaneous tissues, where they might establish an active infection. As the bacteria destroy the tissues under the skin, they might also be carried by the circulation to other organs of the body. The surface of the skin can appear to be normal until late in the disease cycle, making diagnosis difficult. Necrotizing fasciitis is a life-threatening infection, which is frequently fatal.

The Pneumonias

Technically, the term **pneumonia** refers to an acute infection of the lungs, usually caused by bacteria or fungi. It is

usually diagnosed by radiological examination of the lungs. Although pneumonia can develop in those who do not misuse drugs or alcohol, conditions such as alcohol use disorders, immune systems disorders, cigarette smoking, extreme age, vitamin malabsorption syndromes, and malnutrition all can contribute to the development of a pneumonia in a patient. Alcohol use has been linked to greater risk for the development of pneumonia, with a significant amount of research indicating significant risk of respiratory and lung infections in those with AUDs (Yeligar et al., 2016).

Fungal Pneumonia

The development of a fungal pneumonia is a common complication of HIV infection (discussed later in this chapter) and of heroin use (Karch, 2009). Heroin use interferes with the normal function of the immune system, reducing the body's ability to defend itself against these pathogens. But many samples of illicit heroin are also contaminated with fungi, which when injected into the body are transported by the circulation to the lungs, where they might establish an infection site. Fungal pneumonia frequently requires surgical removal of the infected tissues and the use of antibiotic compounds for an extended period of time.

Aspiration Pneumonia

There is a strong relationship between alcohol use disorders and aspiration pneumonia, although many of the other drugs of misuse can also cause this condition. The chronic use of alcohol places the drinker at risk for various forms of lung infection (Kershaw & Guidot, 2008). If the individual should aspirate while regurgitating, she or he would be vulnerable to two different potentially life-threatening dangers. First, the material being regurgitated might be aspirated into the lungs, blocking the air passages. If the drinker is unable to clear the airway in time, hypoxia and possible death may be the result (Johnson & Hirsch, 2003). A second problem is that even if this threat is avoided, some of the material aspirated could start to decompose in the lungs, establishing a growth medium for bacteria.

To further complicate matters, chronic alcohol use alters the normal pattern of bacterial growth in the mouth and throat, again allowing these pathogens access to the lungs if they are aspirated. The respiratory system has few defenses against these microorganisms since they are normally found in other regions of the body. To make things even more complicated, the body's defenses are ill equipped to deal with bacterial growth in the respiratory system of a person whose immune system is often strained by malnutrition and vitamin malabsorption syndromes (Karch, 2009; Marik, 2001).

The true incidence of aspiration pneumonia in the community is not known, since many cases are misdiagnosed as other forms of pneumonia (Johnson & Hirsch, 2003; Lanspa, Jones, Brown, & Dean, 2013). It is known that this is a common problem among people with SUDs, that it is potentially fatal, with greater risk for death than other forms of pneumonia (Lanspa et al., 2013), and that it is always a medical emergency that should be assessed and treated by trained medical professionals.

Community-Acquired Pneumonia (CAP)

Those who use intravenous drugs, smoke cigarettes, and have an alcohol use disorders are all at increased risk for a condition known as CAP (Karch, 2009). Infected individuals will pass the offending bacteria, usually *Streptococcus pneumoniae*, to others through aspiration or inhalation of droplets that form when the person coughs (Musher, 2008). Those who smoke cigarettes are vulnerable to forms of CAP caused by a number of other bacteria, and injecting drugs creates risk to different groups, as does having an AUD (Kaysin & Viera, 2016). People living in close, crowded quarters (such as shelters for the homeless, day-care centers, etc.) are more likely to spread bacteria to those around them (Musher, 2008). People whose immune system has been compromised by malnutrition, vitamin malabsorption syndromes, or conditions that reduce the effectiveness of the immune system such as HIV infection, which reduce the individual's resistance to the offending bacteria, are more likely to contract CAP.

Mild cases of CAP might be treated on an outpatient basis, but eventually many individuals with this condition will require hospitalization, and some will die in spite of medical care. Individuals with comorbid conditions, such as people with an SUD, are more likely to require hospitalization, either for the infection itself or for infection-related complications such as meningitis, endocarditis, etc. Fortunately, a vaccine was introduced in the early 1980s that will provide a degree of protection against *S. pneumoniae*-induced CAP (Musher, 2008).

Tuberculosis

Tuberculosis (TB²) is one of the oldest diseases known to plague humans. Genetic analysis suggests that the bacteria that cause TB first began to evolve 3 million years ago (Lehrman, 2013), and anthropologists have found evidence of tuberculosis at least 500,000 years old (Barry & Cheung, 2009;

Bynum, 2012; Raviglione & O'Brien, 2008; Roth, 2009). In that time, it has been estimated that TB has killed approximately *one billion* people, a number that far surpasses the estimated 40 million deaths around the world caused by the influenza epidemic of 1918–1920, or the total estimated number of deaths caused by the bubonic plague (Roth, 2009). Between the years 1600 and 1900, one in every five deaths in Europe is thought to have been caused by tuberculosis (MacKenzie, 2007). The infection has not become less lethal: At the start of the 21st century, evidence is emerging suggesting that *Mycobacterium tuberculosis* (the bacterium that causes TB) is evolving into new, more virulent forms that are resistant to the antibiotics used to treat the disease (Lehrman, 2013), and now kills more people each year (1.5 million in 2014) than did the AIDS virus (1.2 million in 2014) (“Better detection ups TB numbers,” 2015).

Globally, tuberculosis is widespread: Almost one-third of the world's population is thought to be infected with TB, an additional 10.4 million people contracted the infection in 2015 (World Health Organization, 2016b), and 1.5 million people died from it in 2014 (Bynum, 2012; Lehrman, 2013; “No let up on TB,” 2015; Schurr, 2007; Warner & Mizrahoi, 2014), with an additional 1.4 million deaths in 2015 (World Health Organization, 2016b). Potentially, each infected person might pass the infection to 10–15 other people, maintaining the chain of infection from one generation to the next (Barry & Cheung, 2009). At the start of the 20th century, approximately 50–65% of infected individuals died within 5 years of the initial infection. The introduction of effective antitubercular medications and the development of effective dietary support in the mid-20th century made death from tuberculosis in the United States very rare by the start of the 21st century (Barry & Cheung, 2009; Simon, 2007). Currently, 98% of TB-related deaths occur in the Third World countries, where treatment is difficult or even impossible to obtain (Barry & Cheung, 2009; Raviglione & O'Brien, 2008). In the industrialized countries, many physicians became complacent about the potential for the average person to become infected, which contributes to why the number of people contracting this infection is increasing (Bynum, 2012).

What Is Tuberculosis?

Tuberculosis (TB) is an infection caused by one of the seven known genetically similar strains of *Mycobacterium tuberculosis* (Bynum, 2012; Hauck, Neese, Panchal, & El-Amin, 2009; Lehrman, 2013; Raviglione & O'Brien, 2008; World Health Organization, 2016b). Most strains of *M. tuberculosis* replicate very slowly, and to the consternation of physicians, they have a protein molecule pattern in the cell wall that leaves

²Technically shorthand for *Tubercle bacilis*, although it is generally accepted as an abbreviation for tuberculosis.

them virtually unaffected by many antibiotics used to treat other bacterial infections. *M. tuberculosis* seems to prefer oxygen-rich organs in the body such as the lungs, although cases have been found involving virtually every other organ system in the body (Bynum, 2012; Raviglione & O'Brien, 2008). There is even evidence that *M. tuberculosis* can live without oxygen (Barry & Cheung, 2009).

There are a number of factors that help to determine whether a given individual might develop TB. Environmental factors such as intensity of exposure and malnutrition, combined with the individual's genetic predisposition and poor health, all interact to influence the possibility of a person developing TB (Raviglione & O'Brien, 2008; Schurr, 2007). The greater the number of risk factors a person has, the greater his or her danger of contracting TB upon exposure. There is also preliminary evidence suggesting that dietary or metabolic factors that influence the individual's ability to absorb vitamin D also influence the individual's risk of contracting TB (Wilkinson et al., 2000). Given that individuals with an alcohol or other substance use disorder often have a poor diet, the vitamin D hypothesis might help to explain why this subgroup tends to have be at high risk for TB infection. Paradoxically, obesity seems to offer some degree of protection against tuberculosis (Roth, 2009).

How Is Tuberculosis Transmitted, and How Does It Kill?

The usual mode of transmission is on microscopic droplets of liquid expelled whenever the host sings, talks, coughs, or sneezes. These droplets might remain suspended in midair for extended periods of time, allowing another person to inhale them into the deepest regions of the respiratory system (Bynum, 2012; Markel, 2004). In the healthy individual, the pulmonary defenses destroy or control more than 90% of the inhaled bacteria (Bynum, 2012; Raviglione & O'Brien, 2008). However, in cases where the person's pulmonary defenses are compromised by poor health, malnutrition, or concurrent infection, it becomes more difficult for the body to effectively eject *M. tuberculosis* before it becomes established in the lungs. In these cases, the immune system attempts to mount a counterattack. The initial wave of the immune system response is when the body's macrophages engulf the invading bacteria, surround them, and wall them inside little pockets known as granulomas. In response, the bacteria enter a dormant state within the granulomas where they might remain for years if not decades.

However, if the individual's immune system should become compromised by another infection or malnutrition, the

body loses its ability to keep the bacteria in the granulomas.³ It then becomes possible for the bacteria to burst out and invade the surrounding tissue. This is known as *reactivation* TB, which accounts for a large percentage of all cases of TB in the United States at this time (Lehrman, 2013; Markel, 2004). It is at this point that the body attempts to use a different strategy to attack the invading bacteria: The lymphocytes are called upon to destroy the bacteria. Unfortunately, during this process the lymphocytes also release a toxin that destroys the surrounding tissue, usually the lung tissues. In the case of a TB infection in the lungs, less and less of the lung is able to function properly, and eventually the patient dies of pulmonary failure.

The Treatment of TB

Unfortunately, physicians and public health officials became complacent about TB, and in many cases treatment programs that were effective in essentially eliminating TB in this country in the 1950s and 1960s were rapidly scaled back or eliminated entirely. Then, around the year 1984, health care professionals were stunned to find a growing number of reactivation cases of TB in patients whose infection was formerly latent and often unsuspected by health care professionals (Markel, 2004). Researchers soon discovered that between 10 and 15 million people in the United States had a latent TB infection, providing a "pool" of infected people, each of whom had the potential to infect others should their infection become active again (Hauck et al., 2009; Moyer, 2012).

Several antibiotics have been developed that are effective in treating tuberculosis. However, the bacterium is also evolving in ways that make it resistant to the antibiotics used to treat it (Bynum, 2012; Migliori, De Laco, Besozzi, & Cirillo, 2009). It has been estimated that about 9% of new cases of tuberculosis are resistant to the standard dosing schedule of every known medication used to treat his disorder (Barry & Cheung, 2009; Coughlan, 2012; Migliori et al., 2009).⁴ However, physicians still have a number of medications that they might call upon to treat the average person who has tuberculosis. Thankfully, recent research has changed the typical 20-month treatment to between 9 and 12 months for the

³Bynum (2012) noted that the person who has been infected with tuberculosis has a 5–10% chance of developing an active infection at some point in their lives. The person with an HIV infection has a 5–10% chance of developing an active TB infection *per year* because of their compromised immune system.

⁴Laboratory studies have *suggested* that the use of vitamin C in combination with existing antitubercular medications increases their effectiveness, although this research has not been replicated, and further research to determine whether this phenomenon will work in humans or remain just a laboratory curiosity must be carried out (Vilcheze, Hartman, Weinrick, & Jacobs, 2013).

majority of people (World Health Organization, 2016b). It should be noted that the eradication of an active TB infection does *not* confer any degree of protection against possible re-infection should the person again be exposed to *M. tuberculosis*.

Those who misuse substances are at greater risk for tuberculosis infections. Oeltmann, Kammerer, Pevzner, and Moonan (2009) found that 18.7% of the 28,650 patients infected with TB examined also had a SUD, with alcohol being the most commonly misused substance. Given alcohol's ability to damage the liver, and the fact that many of the medications used to treat TB are metabolized in the liver, this finding has clinical significance for patients currently being treated for this disorder. It might be necessary for the physician to extend the period of active treatment in such patients, according to the authors. Patients with a concurrent SUD were also found to be less likely to adhere to the medication program, and medication adherence must often be monitored by a health care professional to ensure that the patient completes the entire course of treatment. Thus, the SUDs are a significant complicating factor for the treatment of tuberculosis, and threaten to reawaken a plague that once killed millions of people around the world each year in pandemics that have shaped the course of history.⁵

The Viral Infections

The viral infectious process often is confusing to the person who is not a health care professional. Essentially, once a virus particle enters the target cell, it "reprograms" the cell's genetic instructions so that the cell now starts to produce thousands of copies of the virus rather than maintaining normal intracellular function. When the cell ruptures, it releases these viruses into the body, where they then infect other cells. Eventually, hundreds, millions, or even billions of cells are involved in the process of producing new viral particles. Normally, there are two stages to the body's immune system response to a viral infection.

The first time the body is exposed to a new pathogen, it must rely on generalized disease-fighting cells known as **lymphocytes**. These generalist immune system cells roam through the body, seeking out and attacking any cell with a foreign protein pattern in their cell walls. However, while the lymphocytes are staging the initial counterattack against the viral infection, another process is taking place: The body learns to manufacture specific antibodies for the virus so that the body might fight off the infection. Every

species of bacteria, virus, or fungus has a characteristic pattern of protein molecules in the walls of its cells. The immune system learns to recognize the specific molecular pattern in these disease-causing microorganisms, and to attack them. This process may take hours, days, weeks, or in some cases years. After they are formed, however, these antibodies drift through the body, searching for the specific invading pathogens for which they were tailor made, and the person is said to be "immune" to that disease. However, this process is not perfect, and there are several forms of viral infection commonly found in those who misuse alcohol or drugs that can result in permanent infection and massive damage to body organs if not recognized and treated. In this section, we will look at some of the more common forms of such viral infections.

Acquired Immune Deficiency Syndrome (AIDS)

A Short History of AIDS

In 1981, the United States realized a previously unknown disease was spreading (Altman, 1981). Recent research has found that the virus was already in the United States at least 10 years earlier (Gong, Xu, & Han, 2017). In those identified with this disease, the immune system would fail, leaving the person vulnerable to a range of "opportunistic infections."⁶ Initially, this disorder was found mainly in homosexual males, leading to the name *gay-related immune deficiency*, or GRID. Within a short time, the infection began to appear in those who use intravenous drugs and people who had received a blood transfusion, suggesting that it was a previously unknown blood-borne pathogen and not restricted to the homosexual population. By 1982, it was renamed *acquired immune deficiency syndrome*, or AIDS. Shortly afterward, human immunodeficiency virus type 1 (HIV-1) was clarified as the virus that causes AIDS.

The virus is part of the human retrovirus family;⁷ genetic cousins of the human retrovirus family infect sheep, goats, horses, cattle, cats, and monkeys (Fauci & Lane, 2010). It was originally thought that there was just one virus that infected the human immune system, although it has since been recognized that there are two such viruses in this family: HIV-1 and HIV-2. The virus that causes AIDS in

⁵This topic lies outside of the scope of this book, although it is discussed in far more detail in infectious disease textbooks.

⁶It is estimated, for example, that people with HIV infection have a six-fold higher risk for developing a methicillin-resistant *Staphylococcus aureus* infection (MRSA) than those who do not have HIV infection (Popovich, Weinstein, Aroutcheva, Rice, & Hota, 2010).

⁷Subfamily *lentiviruses* if you are interested in such things.

humans is usually referred to as “the AIDS virus” or “HIV” for the most part, although some centers utilize the more correct term HIV-1 or HIV-2, depending on the specific virus causing the infection. Although HIV-2 is generally considered rare in the United States, there has been a more recent spread of this virus from West Africa to India and European countries, as well as the United States (Campbell-Yesufu & Gandhi, 2011).

What Is AIDS?

Technically, AIDS is not a disease in its own right. Rather, it is a *syndrome* induced by the infection with HIV-1 or HIV-2, which ultimately causes the individual's immune system to break down. As the HIV infection progresses, a patient who does not get treatment develops and ultimately dies from a secondary infection, neoplasm, or other condition once easily controlled by the body's immune system.⁸

Where Did HIV Come From?

Scientists now believe that the HIV-1 virus “jumped” from nonhuman primates to humans in Africa between the years 1884 and 1924, although it is possible that in isolated cases humans might have been infected with HIV earlier (Crawford, 2011; “Scientists trace AIDS virus origin to 100 years ago,” 2008). There are a number of other familiar viruses that have also crossed to humans from other animals, such as the Zika virus, Ebola, and severe acute respiratory syndrome (SARS) (Bunduki & Wafula, 2016).

The Scope of HIV Infection

The human immunodeficiency virus is remarkable: In the span of a half century, AIDS has been transformed from an obscure virus found only in isolated areas of Africa to over 36 million people across the globe living with HIV today, and over 1 million dying from AIDS each year (World Health Organization, 2016a). Seventy percent of infected individuals live in sub-Saharan Africa (“U.S. notes AIDS progress, gaps,” 2015). Globally, about half of those people who are infected with HIV are unaware that they are infected, aiding the spread of the virus (Piot & Quinn, 2013; “U.S. notes AIDS progress, gaps,” 2015). The prevalence of HIV infection varies from region to region, with the sub-Saharan region of Africa, Eastern Europe, and the Caribbean having the greatest prevalence of infected adults (Piot & Quinn, 2013).

⁸The antiviral agents currently in use can induce their own constellation of side effects (such as accelerated atherosclerotic changes in the circulatory system), which are technically not induced by the HIV infection itself.

In the United States, around 1.2 million people have been infected with HIV, with less than 13% realizing they have the virus (Centers for Disease Control, 2016b). HIV infection carries with it a significant degree of social stigma, which might express itself through a bidirectional distrust of and by the medical establishment among many of those who are infected (Earnshaw, Bogart, Dovidio, & Williams, 2013; McAteer et al., 2016). Racial disparities also exist in access to treatment resources, contributing to the spread of HIV infection of among previously uninfected populations.

Pediatric AIDS

An unexpected subgroup of persons infected with HIV are those under the age of 18. The fact that most members of society ignore this fact is remarkable, since HIV infection is the seventh most common causes of death for children and adolescents (Van Dyke & Chakraborty, 2013). In the United States, 12,200 of the new cases of HIV in 2010 were in children and adolescents, 59.5% of whom were initially unaware that *they* were infected (Van Dyke & Chakraborty, 2013). Vertical transmission of the infection at birth, sexual contact with an infected partner,⁹ and experimental intravenous drug use are three of the methods through which HIV infection is transmitted. These individuals are often ostracized and socially isolated after revealing that they have HIV, contributing to feelings of depression on their part.

The introduction of effective antiviral medications has resulted in a pool of individuals who were infected as children or adolescents living to adulthood. The therapeutic and social support needs of this population will depend on the individual's level of maturity, intelligence, and age, and will change as the individual matures. A support team comprised of physicians, social workers, and, if the individual has an SUD, a substance rehabilitation counselor will help the individual make the transition from adolescence to young adulthood; however, this step will frequently be difficult for the individual even with this support system.

How Does AIDS Kill?

The AIDS virus differs from many of the traditional viral agents that infect the body. HIV infects the very cells sent out by the body to destroy it: the CD4 cells of the immune system (Bell, 2009). The CD4 cells, also known as the T-helper cells or lymphocytes, are generalists that roam the body looking for foreign invaders (Covington, 2005; Markel, 2004). It has been estimated that following infection between 93 and

⁹Many of whom, as noted, were initially unaware that *they* were infected with HIV.

99% of the total number of HIV viral particles in the person's body are found in the CD4 cells. Small concentrations of the virus particles are found in the cells of the retina, the brain, the testes, and other regions of the body (Pomerantz, 1998, 2003). These sites provide a reservoir of viral particles that might re-infect a person whose body had otherwise been cleansed of the virus (Pomerantz, 1998, 2003).

One of two protein molecules found in the CD4 cell wall is known as the chemokine receptors. Following the introduction of the virus into the body, the virus particle joins with the CD4 cells and injects its own genetic instructions into the cell. In the initial phase of the infection (1–4 weeks from the time of infection) between 50 and 90% of persons will develop nonspecific symptoms of a viral infection (Chu & Selwyn, 2010). These nonspecific symptoms of early-stage HIV infection usually resolve in 2–4 weeks, usually without raising suspicion of a possible new HIV infection. Thirty years ago, it was thought that HIV-1 infection went through a “latency” period. However, it is now recognized that the virus begins to replicate almost immediately after it gains admission to the human body. The so-called latency period was an illusion caused by the fact that early blood tests for HIV infection did not reveal signs of the infection for up to 56 days after the individual contracted the virus (Chu & Selwyn, 2010). Currently, blood tests can reveal signs of HIV infection within 11–15 days of initial infection (Chu & Selwyn, 2010). However, HIV-1 can remain asymptomatic in infected persons for up to 10 years before one of the opportunistic infections caused by the disorder develops, by which time the infection might have progressed to an advanced stage. Indeed, in about 20% of cases, the development of an opportunistic infection(s) is the first sign outward that the person is infected with HIV (Silvestri, 2009).

The HIV-1 virus has developed methods to thwart the body's immune system. First, the HIV-1 virus has been found to have three protein clusters in the viral coat that render it invisible to the body's immune system after it infects a cell (Schaefer, Wonderlich, Roeth, Leonard, & Collins, 2008). One of these proteins also marks the infected cell so that it will not be attacked by the virus a second time, according to the authors. Next, each time the AIDS virus replicates in the victim's body it produces slightly different copies of itself. The specific mechanism for this is quite technical, and well beyond the scope of this text. However, in brief the HIV tends to be “sloppy” during the process of replication, allowing subtle mistakes to slip into the genetic code of each new generation of virus particles. These new “daughter” virus particles are also called “mutations” or “variants” (Forstein, 2002). These variants are released back into the general circulation, but because they do not have the exact molecular pattern of the original viral particle the body must learn to produce

antibodies against these “new” invaders as well. At the end of the person's life the body might have literally billions of slightly different viral particles in his or her body, each of which causes the body to respond to it as if it were a separate virus, overwhelming the immune system. As the immune system weakens, various opportunistic infections once easily controlled by the immune system develop. In many cases, the individual's death is the result of one of the opportunistic infections.

There is also an emerging body of evidence suggesting that persons with HIV infection are at about a twofold higher risk for a heart attack (myocardial infarction) (Freiberg et al., 2013), and also at risk for sudden cardiac death (Tseng et al., 2012). The authors found that persons with an HIV infection were 2.6 to 4.5 times as likely to suffer sudden cardiac death even with low blood viral load counts, although the authors did admit that their study was retrospective in nature, and might overestimate the extent of sudden cardiac death because their sample had a higher percentage of subjects with preexisting heart disease. Still, this is an area that warrants further research to identify the causal mechanism and possible treatments. Another risk factor for HIV progression is whether the infected person smokes cigarettes, which appears to accelerate the progression of the AIDS virus in the infected person for unknown reasons.

The Chain of HIV Infection

In spite of its reputation, HIV is a rather fragile virus, and is not easily transmitted from one person to another (Oldstone, 2010). There are several methods of HIV transmission: Male-to-male sexual contact is the most common method of HIV transmission in the United States at this time, accounting for 67% of all diagnoses (Centers for Disease Control, 2016b). Receptive anal intercourse is an effective method of HIV transmission, since the microscopic tears in rectal tissues provide the virus with access to the bloodstream of the receptive partner. It has been estimated that the odds of contracting HIV from receptive anal intercourse with an infected partner are as high as 1:10 (Mayer, Skeer, & Mimiaga, 2010). Unprotected heterosexual intercourse (where only one partner is infected with HIV) is the second most common method of HIV transmission, although vaginal intercourse is not a very effective method of HIV transmission. The odds of contracting HIV after a single unprotected coital act with an infected partner has been estimated to be approximately 1:2,000 (Mayer, Skeer, & Mimiaga, 2010). Obviously, repeated sexual contact with an infected partner increases the odds of viral transmission to the uninfected partner. Seventy-five percent of women who have contracted HIV infection are thought to have done so as a result of unprotected sexual

activity with an infected partner. Recent research has indicated that the use of methamphetamine and other synthetic amphetamines, use of drugs of any kind intravenously, and use of drugs to facilitate sexual activity are associated with increased likelihood of HIV (Bowden-Jones et al., 2017).

The sharing of intravenous needles by those using drugs is the third most common method of disease transmission in the United States at this time (“HIV infection among injection drug users—34 states, 2004–2007,” 2010). HIV infection among those using intravenous drugs has been reported in 120 countries around the world (Arasteh & des Jarlais, 2008), and it has been estimated that approximately 40% of individuals who use intravenous drugs are infected with HIV (MacArthur et al., 2012). In the United States, there has been an 80% drop in the number of people who contract HIV through shared intravenous needles, which is a tribute to the effectiveness of harm reduction efforts (Centers for Disease Control and Prevention, 2009a). The development of appropriate blood screening tests has made HIV transmission via transfusion or use of blood products in medical procedures very rare.¹⁰

A less common method of HIV transmission is known as “vertical transmission.” During this process an infected woman passes the virus on to her baby, usually during childbirth. The odds of vertical transmission are reduced to less than 1% if the mother is fully compliant with an aggressive antiviral medication regimen (Havens, 2009; Rhame, 2009). It is also possible for the mother to infect the infant through breast feeding (Fauci & Lane, 2008). The risk for a health care worker who suffers an accidental needle stick has been estimated at between 0.3 and 0.9% (Fauci & Lane, 2008; Longo & Fauci, 2008).

Life Expectancy for People with HIV-1 Infection

Before the development of effective antiviral medications for HIV, the mean survival time after the person contracted this viral infection was 10 years (Cooper, 2008). About 10% of those people who were infected were “rapid progressors,” who developed AIDS within 5 years of infection, while about 10% of those infected were “slow progressors,” who took an exceptionally long time to progress to AIDS.¹¹ While great strides have been made in developing medications that will slow the replication of the virus, even with the best antiviral treatments available, the average HIV-infected person is

thought to lose ten potential years of life (Cooper, 2008).¹² HIV-positive individuals who have an alcohol use disorder appear to pass through the various stages of the infection more rapidly (Bagby, Amdee, Siggins, Molina, Nelson, & Veazey, 2015). The infected person who is also an active intravenous drug addict is thought to lose approximately 20 years of potential life span to the combined effects of HIV infection and their SUD (Cooper, 2008).

There is a very small subgroup (approximately one out of every 300 infected persons) whose bodies seem to have fought the infection to a standstill (Walker, 2012). Their bodies still carry the virus, but the bodies of these individuals appear to be able to hold the virus at bay, preventing it from progressing further (Walker, 2012). Scientists are trying to isolate the protective factor in their blood to determine whether it might be a potential treatment approach for this disease.

The Treatment of HIV Infection

There are efforts to develop a vaccine to prevent HIV infection, but these efforts are still ongoing (Berneman, 2016). One of the most important factors in the treatment of HIV infection is early detection, so that antiviral therapies can be initiated. Unfortunately, HIV is spreading far more rapidly than people are being placed on antiviral therapy regimens (Coghlan & MacKenzie, 2011). One reflection of this fact is that it is not uncommon HIV infection to be detected only about 1–3 years before the onset of AIDS (Carr & Lynfield, 2009; Shouse et al., 2009). This reflects, in part, the complacency that has developed in the general public, who have mistakenly come to believe that HIV/AIDS no longer presents a threat to the individual.¹³

Once a person is infected, a very important component of HIV treatment is the patient’s nutritional status (Hendricks & Gorbach, 2009). Individuals who use intravenous drugs typically lack access to adequate food sources, and even when appropriate food is ingested, illicit drugs can interfere with the absorption of many vitamins and minerals needed for adequate health (Hendricks & Gorbach, 2009). One such micronutrient is *selenium*. Individuals who took a selenium supplement as prescribed were found to have no increase in viral load levels, and an increase in the CD4 T cell count (Hurwitz et al., 2007). The authors concluded that daily supplementation of the individual’s diet with selenium

¹⁰Rhame (2009) reported that this route of transmission in the United States has been “virtually eliminated” (p. 38) as a result of rigorous blood testing prior to transfusion.

¹¹The introduction of effective antiviral treatments made it impossible to determine the median survival time for slow progressors.

¹²This figure assumes that the person has been infected with HIV just once. There is strong evidence suggesting that subsequent infections with HIV from other sources (infected sexual partner or intravenous drug use involving an IV needle shared with an infected person) might accelerate the progression of HIV to the stage of AIDS (Smith et al., 2004).

¹³It also reflects the average time between initial infection and when the first blood test for HIV infection is carried out, as few people suspect infection in the early stages of HIV infection.

was an inexpensive way to both suppress the virus replication process and increase the CD4 T cell count. Further research into the impact of dietary malabsorption syndromes on the health status of HIV-infected patients is necessary.

Pharmaceutical companies have developed an ever-growing number of antiviral agents to assist in the fight against AIDS, turning what was once a virtual death sentence into a chronic but treatable infectious disease. Unfortunately, (1) these compounds slow but do not eliminate the replication of HIV, and (2) the high cost of obtaining these medications prohibits some people from being treated (Craig, 2004). To combat the problem of viral resistance to the antiviral medication(s), physicians simultaneously prescribe medications from different classes of antivirals (Henry, Alozie, & Bonham, 2009). Once termed HAART (“highly active antiretroviral therapy”), this treatment format is often referred to as cART (“combination antiretroviral therapy”).

Medication noncompliance is the main reason why cART is less than 100% effective. It has been estimated that the patient must take a minimum of 80–90% of the prescribed medication doses at the proper time to achieve maximum effect and limit the development of strains of HIV that are resistant to the medications (Scott & Marcotte, 2010). The team of Barclay, Wright, and Hinkin (2010) offered an even higher figure of 90–95% compliance being necessary to achieve the highest degree of viral suppression. Unfortunately, up to 40% of patients on HAART medication programs are not compliant with taking their medications as prescribed, in part because of their harsh side effects. Another reason for treatment noncompliance is the concurrent use and misuse of recreational chemicals. Even “sub-hazardous” level of alcohol use is associated with a lower level of treatment compliance and increased mortality (Braithwaite & Bryant, 2010, p. 285). Other reasons for treatment noncompliance include those persons who are depressed, or who have unrealistic expectations for the treatment process.

While antiviral medications might slow the replication of HIV in the human body, they do not eliminate the virus from the body. To date, the complete eradication of HIV from the body remains a goal that has not been achieved. To accomplish this, it would be necessary to eliminate every HIV virus particle found in the body, including those within infected cells, to achieve a total cure, a goal that to date remains elusive (Cohen, 2015). In theory, new treatment methods could prevent the spread of HIV and hint at the possibility of a cure in the distant future (Coghlan & MacKenzie, 2011).

AIDS and Suicide

There is a great deal of controversy about the relationship between HIV infection and suicide. It is currently thought that

individuals infected with the AIDS virus who are receiving adequate antiviral therapy are three times as likely to commit suicide as an uninfected person the same age (Carrico, 2010). The period of greatest risk appears to be the period immediately after the individual learns that he or she has been infected with the virus. It is thus recommended that a suicide risk assessment be carried out with each patient with HIV and periodically after treatment has started, and that comorbid psychiatric conditions be addressed (Carrico, 2010).

AIDS and Neurocognitive Dysfunction

Shortly after the individual is infected with the HIV virus, it enters the brain, where the virus is able to cause inflammation and the accumulation of neurotoxic compounds such as the cytokines. This in turn will activate the brain's defensive immune response system, resulting in the destruction of both neurons and glial cells (Fauci & Lane, 2010; Scott & Marcotte, 2010). This appears to be the mechanism for neurocognitive problems that are found in at least 50% of people infected with HIV (Scott & Marcotte, 2010). The degree of neurocognitive deficit can range from very mild to severe, and degrees were classified by Scott and Marcotte (2010) as follows:

Asymptomatic: Neuropsychological test performance at least two standard deviations below expectations in two of five areas assessed, but patient retains ability to carry out ADLs.¹⁴

Minor neurocognitive deficits: In addition to the above criteria, the individual does have a mild impairment in their ability to carry out ADLs but does not meet the criteria for dementia.

HIV-associated dementia: Neuropsychological test scores that are at least two standard deviations below norms on two of the five areas assessed for the individual, and marked impairment in their ability to carry out ADLs.

Strict medication adherence has been found to reduce the probability that the individual will develop HIV-related neurocognitive problems, or at least the severity of such deficits if they develop (Scott & Marcotte, 2010).

HIV Infection and Employment

It has been estimated that HIV infection results in a \$22,000 a year reduction in earning potential for the individual (Scott & Marcotte, 2010). Since many insurance companies are

¹⁴Activities of daily living. See Glossary.

unwilling to pay for the high cost of programs such as HAART/cART, individuals who are infected with HIV often must stop working and turn to programs as Social Security so that their medications will be paid for by other agencies.

HIV and Mood Disorders

Depression is common among persons with HIV, but care should be taken to differentiate between the individual being demoralized because of their health status, bereavement over the loss of friends and loved ones to HIV, accidents, or other diseases, and actual depression (Cohen, 2013). Cohen (2013) also suggested that posttraumatic stress disorder is common among patients who carry the AIDS virus; however, there has been little other research suggesting that this is true.

Section Summary

Acquired immune deficiency syndrome (AIDS) has been identified as the end stage of a viral infection caused by the human immunodeficiency virus (HIV), a blood-borne virus that is a member of a family of viruses that share certain common characteristics. Over time, different members of the HIV family of viruses have been identified, which are now identified by numbers (HIV-1, HIV-2, etc.). AIDS is now known to be the end stage of an infection by either HIV-1 or, more rarely, HIV-2 (Lashley, 2006). Initially, infection with either virus was a virtual death sentence, and prior to the introduction of effective antiviral medications the average survival period between initial infection and death from an opportunistic infection(s) was approximately 10 years. The new antiviral medications have transformed HIV infection from a virtual death sentence to a chronic disease that can be controlled, like diabetes or heart disease, and there is a glimmer of hope that it might be possible to cure an infected person of this disease, although this remains a very distant goal.

Viral Hepatitis

The root *hepa* refers to the liver, while *-itis* denotes an inflammation of the specified organ system. Thus, the term *hepatitis* is a general term that means inflammation of the liver, which then must be qualified by the causal agent such as “alcohol-induced hepatitis” or “toxin-induced hepatitis,” etc. Viral hepatitis refers to an inflammation of the liver induced by any of a number of different viral agents (Orr, 2008). In this section, we will briefly discuss some of the forms of viral hepatitis commonly encountered in the treatment of people with an SUD. To better classify them, scientists have labeled each of the viral agents that can induce hepatitis by a letter.

A Brief History of Viral Hepatitis

Physicians have long known that if a person were to be exposed to water or food contaminated by fecal matter, he or she might become ill with any of a wide variety of diseases.¹⁵ It was only in the 20th century that physicians began to understand that there were viral pathogens that might attack the liver. The first such virus to be identified was initially called just “viral hepatitis.” But physicians were also aware that some patients developed hepatitis after receiving a blood transfusion, a condition that they began to call “serum hepatitis.” In 1966, a virus that was classified as *hepatitis type B* (HBV) was isolated. Unfortunately, it was soon discovered that HAV and HBV could not explain every case of what appeared to be viral hepatitis. It was hypothesized that yet another, undiscovered, virus could also cause viral hepatitis in humans, and patients with hepatitis who did not appear to have either type A or type B hepatitis were said to have “non-A/non-B” hepatitis. Since then, additional viruses that could infect the human liver have been identified, which are now classified as hepatitis type C (HCV), hepatitis type D (HDV), and hepatitis type E (HEV). Viral hepatitis kills 1.4 million people each year and infects between 6 and 10 million new people each year, with a total of 400 million infected persons across the globe (World Health Organization, 2017a).

Hepatitis A Virus

METHOD OF TRANSMISSION

Viral hepatitis caused by the A virus (HAV) most commonly is transmitted by oral-fecal transmission¹⁶ (Centers for Disease Control, 2015b; Orr, 2008), although some cases involve the sharing of a contaminated intravenous drug needle. A person might be exposed to the virus by changing a diaper that is contaminated by fecal matter, changing contaminated bed linens from a bed where an infected person was resting, and then failing to wash his or her hands. Other methods of transmission include swimming in contaminated water or eating food products that have not been properly cooked to ensure the death of pathogens. Proper hand-washing, appropriate food preparation, and not sharing intravenous needles are all ways to avoid exposure to the hepatitis A virus.

SYNDROME INDUCED BY HAV

After exposure to HAV, the individual will usually experience a flu-like syndrome for about 4 weeks, although in 1%

¹⁵Cholera is another example of a disease that might be contracted through contact with water contaminated with fecal material.

¹⁶Which is one reason why washing your hands after using the toilet is so important.

of cases the individual develops acute liver failure (Fontana, 2008). This is usually seen in older adults who contract HAV, but it can occur in younger patients as well (Dienstag, 2008). The individual remains contagious throughout the period in which he or she demonstrates symptoms of HAV infection, after which time she or he will have lifelong immunity to the virus (Orr, 2008).

CONSEQUENCES OF HAV INFECTION

HAV tends to be a time-limited disorder, which in very rare cases can result in liver failure and the patient's death. Also, a patient may develop *relapsing hepatitis* in the weeks or months after apparent recovery. This is rare, but if it does develop the patient will re-experience many of the symptoms of the original infection (Dienstag, 2008). This second episode is a manifestation of the original infection that has not fully resolved. Hepatitis A viral particles have been found in fecal matter of people experiencing relapsing HAV, suggesting that they remain infectious during this time. Once the patient recovers from the HAV infection, she or he will have lifelong immunity to this virus.

Hepatitis "B" Virus

METHOD OF TRANSMISSION

The virus that causes hepatitis type B (HBV) has six known subtypes, all of which are quite contagious. It has been estimated that this virus is 100 times as contagious as the virus that causes HIV infection. Although the virus that causes AIDS will die within minutes after exposure to air, scientists believe that HBV can continue to live on contaminated surfaces such as counter tops, etc. for 7 days or more after being deposited there by an infected person if the surface is not properly cleaned (World Health Organization, 2016c).

The hepatitis B virus is a blood-borne disease, which requires exposure to the body fluids of an infected person. Known methods of hepatitis B transmission include sharing a toothbrush or a razor, sexual contact with an infected partner, or even by simply kissing an infected person. The virus can be transmitted through blood transfusions, although blood donations are now screened for donors, and the rate of infection is less than 1 case for every 250,000 units of blood administered. Because it can be contracted as a result of sexual intercourse, HBV is often classified as a sexually transmitted disease (STD) as well as a blood-borne pathogen.¹⁷ HBV vertical transmission from an infected mother to an infant during childbirth is possible, resulting in a low-grade lifelong infection for the baby following birth. This is the result of the "immunologic tolerance" that the baby's body

develops for the virus (Dienstag, 2008, p. 1938). In spite of this immunologic tolerance, HBV infection may culminate in liver failure decades later in life (Dienstag, 2008).

Another common method of HBV transmission in the United States is the sharing of intravenous needles between those using drugs.¹⁸ Globally, 22 million new cases of HBV develop each year because of the sharing or reuse of contaminated needles (White, 2011). Those who use intravenous drugs in a prison setting often try to avoid this by making the "yellow guy"¹⁹ use the needle last, ignoring the fact that virus particles still will remain in the needle when it is next used, hours or days later, thus passing the infection on to the next user.

SYNDROME INDUCED BY HBV INFECTION

Individuals who have been infected by HBV might not demonstrate outward symptoms of an infection for 1–5 months after exposure, although blood tests will demonstrate an immune response to HBV within 1–12 weeks of the initial infection. The physical symptoms that eventually develop are similar to those seen with hepatitis A infection, and will include such symptoms as anorexia, nausea, vomiting, fatigue, malaise, headache, photophobia, pharyngitis, and cough, followed 1–2 weeks later by symptoms of jaundice as the virus attacks the liver (Dienstag, 2008). These symptoms usually continue for 4–6 weeks, but on rare occasions they can continue for as long as 4–12 months following infection. Once the individual has recovered from HBV infection, she or he is immune to the virus, and blood tests will reveal HBV-specific antibodies for the rest of the individual's life (Orr, 2008).

CONSEQUENCES OF HBV INFECTION

The prognosis for a healthy adult who contracts HBV is usually seen as quite favorable, and it has been suggested that 90–95% of previously healthy adults eventually recover completely (Dienstag, 2008). This figure was disputed by Pungpapong, Kim, and Poterucha (2007), who utilized DNA testing procedures and reported that they found traces of HBV in people who were thought to be virus-free up to a decade after the acute infection resolved. The World Health Organization (2016c) indicated that less than 5% of healthy adults will end up with chronic HBV, but children are much more at risk: Up to 90% of those infected before age 1 will develop chronic HBV, whereas up to 50% of children infected before age 6 will develop chronic HBV.

One of the more dangerous consequences of HBV infection is acute liver failure. This complication from

¹⁷Which is to say that the virus is found in all body fluids.

¹⁸It is interesting to observe that in spite of this information only 68% of substance rehabilitation programs offer either on-site blood testing or have contractual agreements with private health care providers who will perform these tests for persons who enter treatment (Bini et al., 2012).

¹⁹Which is to say the guy who has jaundice.

hepatitis B infection has been estimated to develop in less than 1% of cases that occur in healthy adults (Fontana, 2008). However, the rate of fulminant liver failure in HBV patients is markedly increased if the individual should also have contracted the hepatitis D virus as well (Dienstag, 2008).²⁰

The issue of whether the typical patient completely recovers from an acute HBV infection is unresolved, and physicians argue over whether the virus is ever completely eliminated from the body of an infected individual. One of the manifestations of chronic infection with the hepatitis B virus is the slow destruction of the patient's liver (Ganem & Prince, 2004; Pungpapong et al., 2007; Russo, 2004). Between 20 and 30% of patients with a long-term HBV infection will develop cirrhosis of the liver and/or liver cancer (World Health Organization, 2016c).

It was once thought that the virus directly caused the death of liver cells, but recent evidence has suggested that it is the body's immune response to the HBV infection that causes the liver damage rather than the virus itself (Dienstag, 2008; Ganem & Prince, 2004). Long-term HBV infection also is an indirect cause of death, as evidenced by the fact that people who have contracted HBV are 10–390 times more likely to develop liver cancer than a non-infected person (Ganem & Prince, 2004; Gordon, 2000; Orr, 2008). Liver cancer is difficult to detect and treat, and it is usually fatal.

As if that were not enough, there is evidence to suggest that even if the individual were to recover from HBV infection, he or she is 2–4 times as likely as normal to develop cancer of the pancreas (Hassan et al., 2008). The causal mechanism for this is not known. People who were diabetic and who had past exposure to HBV were found to be seven times as likely to develop cancer of the pancreas as people without either disorder, according to the authors.

TREATMENT OF HBV INFECTION

Currently, the most effective “treatment” for HBV infection is prevention. Vaccines to prime the immune system against HBV infection have been developed and are recommended for people who might be exposed to this virus, such as health care workers, the spouse of an infected person, children, and adolescents. Some school districts require proof of vaccination before allowing students to enter school for the academic year. Blood barrier precautions (gloves when handling blood products or other body fluids) are also helpful in preventing HBV transmission. A number of antivirals have been investigated as possible treatments for those who are already

infected with HBV, with extensive guidelines for medical professionals for use in different age groups and circumstances (Terrault et al., 2015).

Hepatitis “C” Virus

MODE OF TRANSMISSION

It has been estimated that up to 150 million people worldwide (World Health Organization, 2016d), and up to 3.9 million people in the United States, have a chronic hepatitis C (HCV; also called Hep C) infection (Centers for Disease Control, 2017; Sostre & Tiu, 2013; Wapner, 2015). A great deal has been discovered about this virus since it was first isolated in 1989. First, 8,500 blood samples drawn from troops at a U.S. Army Air Force²¹ base for penicillin research between 1948 and 1954 were kept in a frozen state, then thawed and tested for HCVV. Seventeen of the samples tested positive for the virus, demonstrating that it had arrived in this country at least 40 years before it was first identified (Wapner, 2015). It has also been discovered that the virus has at least six genotypes and more than 50 subtypes (Centers for Disease Control, 2017). The virus is thought to be 10 times as infectious as the HIV virus and is classified as a blood-borne pathogen (Mehta et al., 2011). In the United States, HCV infections take more lives than does HIV each year (Ly et al., 2012). Those who use intravenous drug make up the largest proportion of new cases of HCV (Centers for Disease Control, 2017), although researchers disagree about the exact percentage of new cases found in this subpopulation. Williams, Bell, Kuhnert, and Alter (2011) offered an estimate of 45% of new cases being attributable to intravenous drug use, while Sostre and Tiu (2013) suggested that 65–70% of new cases of HCV infection occur in those who use intravenous drugs. There has been a modest drop in the number of new cases of HCV infection due to needle exchange programs in some communities.

Unfortunately, many individuals who shared an intravenous needle only once or twice in their late teens or early twenties are now discovering that this experiment had unanticipated long-term health consequences. Further, HCV can be transmitted through sexual contact with an infected partner, or through used tattoo needles (Davies, 2005; Wilkins, Malcolm, Raina, & Schade, 2010). Other sources of HCV infection include organ transplants from infected donors and occupational exposure to blood products, such as hemodialysis workers who might contract the infection as a result of exposure to blood products at work (Dienstag, 2008).

²⁰It has been estimated that only 28% of substance rehabilitation programs offered blood testing for HBV either on-site or through contractual agreements with health care providers off site (Bini et al., 2012).

²¹What is now the U.S. Air Force was part of the U.S. Army and did not become a separate branch of the armed forces of this country until after the end of World War II.

Approximately 10% of HCV victims contracted the virus before the advent of effective blood screening methods for blood donors. Currently, the risk of contracting HCV through a blood transfusion has been estimated at 1:2,300,000 (Dienstag, 2008). The HCV virus can also remain on surfaces and still be infectious for up to 4 days unless the contaminated surface is disinfected.²² Another possible route of infection might be the shared use of straws to inhale cocaine, although this is controversial and has not been proven to be a route of HCV transmission.

CONSEQUENCES OF HCV INFECTION

The acute period of illness following infection with HCV is less severe than that seen with HAV or HBV (Dienstag, 2008), and there is no disease-specific syndrome to alert medical staff that an individual has been exposed to the virus. Approximately 20% of persons infected with HCV are able to overcome the virus, usually within the first 6 months, after which they are virus-free²³ (Davies, 2005; Hines, 2002; Sostre & Tiu, 2013; Woods & Herrera, 2002). However, whereas it was once thought that in the remaining cases, HCV would establish a smoldering infection that would slowly destroy the individual's liver over a period of 20–30 years, it has since been discovered that severe consequences of HCV infection develop only in about one-third of persons infected with this virus (Wapner, 2015). The problem is that we do not know how to identify which persons are at greatest risk for HCV-related liver damage as opposed to developing a chronic asymptomatic infection or being able to overcome the virus without treatment.

One problem facing physicians is that infected persons who do progress to developing severe liver damage remain asymptomatic until the level of liver damage begins to manifest. Early identification of these individuals is essential because up to 70% of individuals who develop acute liver failure during the initial stage of HCV will succumb to liver failure in the more advanced stages of the infection (Fontana, 2008), and that for unknown reasons 1–5% of persons with an active infection will develop liver cancer each year (Orr, 2008).

In many cases, the infected individual might live for 20–30 years before the cumulative level of damage to their liver results in acute liver failure, and at this point an emergency liver transplant might be the only hope of saving the patient's life (Davies, 2005). HCV-induced liver damage is the most common reason for liver transplantation in the United

States at this time (Orr, 2008). Many persons infected with HCV continue to misuse of alcohol or illicit drugs (Sostre & Tiu, 2013). Unfortunately, it has been shown that individuals with an alcohol use disorder or who misuse marijuana seem to progress through the different stages of the disease more quickly than individuals who abstain from alcohol and marijuana. For this reason, alcohol and marijuana use are absolutely contraindicated for people with HCV infection (Karsan, Rojter, & Saab, 2004; Sylvestre, 2008; Wilkins et al., 2010).

TREATMENT OF HCV INFECTION

There is no vaccine that will prevent HCV infection (World Health Organization, 2016d; Wilkins et al., 2010). The most effective prevention methods for HCV infection are the use of barrier precautions to prevent direct exposure to blood products, cleansing of surface areas that are potentially contaminated by the virus, and not sharing intravenous needles with others. Nine out of ten individuals who have been identified as having HCV are cured through the use of antiviral medications, but the number of people who access care to be identified and treated is low (World Health Organization, 2016d), thus resulting in a cycle of infection.

Hepatitis D

These viral infections are only rarely found in the United States (Centers for Disease Control, 2015c). Of the estimated 15 million people with hepatitis D (HDV) around the world (World Health Organization, 2016e), 70,000 are thought to live in the United States, with 5,000 new cases of HDV developing each year in this country (Karsan et al., 2004). It is interesting to note that HDV is an “incomplete” virus, which requires a concurrent infection by the hepatitis B virus to be able to infect the host. Since the largest proportion of people infected with HBV contracted that infection through contaminated intravenous needles, it should not be surprising to learn that many individuals who misuse drugs with hepatitis B have also been exposed to HDV at some point in their lives. Proper vaccination against HBV appears to have the added benefit of blocking HDV infection as well.

Hepatitis E

Hepatitis type E has received scant attention in the medical literature despite the fact that possibly a third of the world's population has been exposed to this virus (Zhu et al., 2010). It is most prevalent in Eastern and Southern Asia (World Health Organization, 2016f). The HEV virus can be transmitted through direct contact with feces, although the most common method of transmission of HEV appears to be exposure to water contaminated by a person infected

²²A fact which makes you want to think twice about using public toilets, does it not?

²³They *will*, however, continue to test positive on blood tests that only screen for antibodies to a specific virus. There is a need for follow-up testing to determine whether a specific individual has an active HCV infection.

with HEV (World Health Organization, 2016f). If infected, the only treatment for the patient is supportive medical care. However, a vaccine has been developed for HEV that is both effective and safe to administer (Zhu et al., 2010), but at this time it is only available in China (World Health Organization, 2016).

Chapter Summary

Those who misuse substances are at high risk for a wide range of infectious diseases, both as a direct result of their substance use and as an indirect consequence of their SUD. Individuals who share intravenous needles spread pathogens from one person to the next. The failure to follow sterile technique often results in the individual using intravenous

drugs “punching in” pathogens normally found only on the surface of the skin, and these bacteria and fungi then infect the person. This is an example of an indirect infectious disease consequence of injected drug use. Malnutrition that is a side effect of drug use disorders also is an indirect cause of infectious diseases in those who inject drugs.

People with alcohol use disorders share the dangers of malnutrition as a possible risk factor for infections. However, they are also at risk for aspiration of material being regurgitated, setting the stage for aspiration pneumonia. Injecting drugs with contaminated needles also puts the person at risk for viral, fungal, and bacterial infections not normally found in the humans. These disorders include HIV infection and the various forms of infectious hepatitis. All of these disorders have the potential to kill the patient without (and sometimes even with) the best of medical care.



CHAPTER 37

The Debate over Drugs

The Relationship Between Drug Use and Crime

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 37.1** Understand the history of Prohibition and the impact on the world today
- 37.2** Consider the pathways between criminal activity and SUDs
- 37.3** Review the connection between drug use and violence
- 37.4** Describe the impact of adulterants in relation to drugs
- 37.5** Review what is currently known related to designer drugs and drug analogs

Introduction

In his science fiction classic *I will Fear No Evil*, Robert A. Heinlein (1970) introduced the concept of the *Abandoned Area*. This is an urban area in which poverty, crime, the deterioration of the infrastructure, and drug use were so rampant that the government just gave up on these areas. Laws were ignored within these zones, and illicit drug use was so rampant as to appear to be the norm rather than the exception. Virtually any drug or service could be obtained within an Abandoned Area for the right price. Amazingly, this science fiction portrayal of a fictional world appears to have presaged the state of affairs in much of the Western world a half century later.¹ In this chapter, the relationship between substance use disorders and crime will briefly be explored.

Harry Anslinger²

Arguably, Harry Anslinger³ is perhaps the individual who is most responsible for shaping drug control policy in the United States, and although he passed away in 1975, his influence in shaping drug control policy in this country is still being felt. He was a strong supporter of prosecution and

¹If you wish to challenge this assertion, please do so only after spending 24 hours living on the streets of the ghetto area of any number of cities in the United States alone.

²Born May 20, 1893; died November 14, 1975

³Entire books have been published about Mr. Anslinger's life and his impact on the "war on drugs," and the reader is referred to these biographies if they wish to learn more about him.

incarceration of those who violated the laws prohibiting the use of designated chemicals. In 1929, he was appointed an assistant to the commissioner of the U.S. Bureau of Prohibition. The country was in the midst of the “Great Experiment,”⁴ in which alcohol use was prohibited. The Bureau of Prohibition was charged with enforcing these laws, although there were almost daily revelations about scandals, bribery, and corruption⁵ in the agency.⁶ In spite of these revelations of wrongdoing within the Bureau of Prohibition, Harry Anslinger was acknowledged as an honest, incorruptible law enforcement officer. With the end of the Prohibition he was appointed to the position of director of the Federal Bureau of Narcotics (BON). It is rumored that he became jealous of J. Edgar Hoover’s growing power and prestige as the director of the Federal Bureau of Investigation (FBI) and worked to make the BON an equally powerful agency in the federal government.

Harry Anslinger and the BON did not focus all of their energy on alcohol; they also devoted time to the problem of addiction to narcotics, a term that was applied to a wide range of chemicals that technically were not narcotics. However, he did focus a great deal of time and energy on trying to alert the country to the “danger” of a hidden “epidemic” of marijuana abuse. There was no epidemic of marijuana abuse, so he had to (a) alert the country to this nonexistent epidemic and then (b) “educate” the public to the dangers of marijuana use. He did this through an elaborate campaign of radio interviews, newspaper articles, and the occasional appearance before a congressional subcommittee. At every opportunity, he railed against the dangers of marijuana and other drug use. In newspaper interviews he would illustrate the loss of control brought on by marijuana, citing unspecified police reports of criminal cases in which children were alleged to have committed heinous crimes such as killing various family members after having used marijuana.⁷ Many of these reports were made up, or the evidence suggested that the perpetrator had used marijuana weeks or months before the crime was committed, a fact that he failed to mention during the interview. He also was not above using racism as a part of his campaign, hinting to southern members of Congress that Negroes⁸ made up a disproportionate percentage of

marijuana users (Hari, 2015) and that it could cause them to lose control and start raping white women. Such use of misinformation has remained an almost unspoken policy of entire agencies on the local, state, and federal levels when they discuss drug abuse, and it can be traced back to Harry Anslinger’s rise to power (Szalavitz, 2005).

Anslinger labeled research that contradicted his preconceptions as unscientific in their conclusions.⁹ All of this reflected his core belief that the brains of the person with an SUD had been hijacked by the chemical forever and that they should be locked away from the rest of civilized society (Hari, 2015). The legal system offered him a way to isolate society from those who misused chemicals, people he viewed as being lower than the rest of society (Hari, 2015). Through his work, the substance use disorders were transformed from a medical condition into a legal problem presenting society with a conundrum: If substance use disorders are identified as a medical or psychiatric disorder, why is one of the treatments for this disorder incarceration, according to the law? Society has ignored this apparent contradiction and has continued to consider legal sanctions as the main tool against the substance use disorders.

The Lessons of History

As Harry Anslinger discovered during Prohibition, it is virtually impossible to block the flow of a proscribed chemical into this country. Some even questioned the need for Prohibition since the per capita consumption of beer in the United States reached its lowest level between 1911 and 1914, before the Volstead Act became law (Schweikart, 2008). The number of deaths from cirrhosis of the liver reached its lowest level in 1921, just a year after the start of Prohibition.¹⁰ By the end of Prohibition, medical journal articles on alcohol had all but disappeared (Schweikart, 2008). Admittedly, the level of alcohol consumption fell during the Prohibition years, but only by approximately 30% (Okrent, 2010; Schweikart, 2008).

People who wanted to drink found ways to obtain alcohol. Agencies either under Anslinger’s direct control or in cooperation with the U.S. Bureau of Prohibition attempted to interdict

⁴Technically the law was called the Volstead Act of 1919.

⁵Many could, by calling in “sick” on certain specific nights, earn as much in bribes for being sick that one night as their regular job paid in a year (Okrent, 2010).

⁶Of course, many members of Congress continued to drink, being supplied with the best of the alcohol seized by the Coast Guard and other law enforcement agencies.

⁷The media usually did not check on the veracity of these reports but accepted them without question.

⁸This term, while not “politically correct,” is the term that was used in Anslinger’s time.

⁹An excellent example of this is how he dismissed the final report of a study carried out at the request of the mayor of New York City, Fiorello La Guardia. The report was submitted by the New York Academy of Sciences in 1944, after 4 years of research; it contradicted the government’s claim that marijuana use caused insanity or that it played a role in the commission of major crimes. Anslinger promptly labeled the study as unscientific and ordered that no further research on marijuana be carried out without his express approval.

¹⁰It takes a number of years of chronic alcohol use for liver cirrhosis to develop. The fact that deaths from cirrhosis reached the low point in 1921 is indirect evidence that alcohol use had been falling before the start of the Prohibition in 1920.

the flow of alcohol into this country from overseas. State and local officials focused their efforts on domestically produced sources of alcohol. One unintended side effect of Prohibition was the development of the sport that is now embodied in NASCAR.¹¹ Local law enforcement agencies would try to stop delivery vehicles carrying liquor from illegal distilleries, and the drivers of these vehicles would naturally try to escape the authorities by modifying their vehicles to make them faster.

Supply ships would journey to Canada or Mexico, where the purchase of alcohol was legal, and stock up on various brands of liquor. Then these ships would anchor just outside of the territorial waters of the United States, beyond the reach of the Coast Guard and other federal law enforcement agencies. These ships would then act as supply nodes for smaller boats that would pull up alongside and present a shopping list of the different types of liquor their customers desired. The supply ships would provide the desired number of cases of the desired liquor for a fee that was higher than what the same liquor cost in the country of origin. The supply ships rationalized such high prices as being necessary to pay for the ship's maintenance, crew salaries, what they had to pay their overseas supplier, the risk of arrest that they were taking, etc.

The owners of these boats would in turn transport the liquor to shore in small boats,¹² which would race to identified landing points where the cases of liquor would change hands yet again for a slightly higher fee. Waiting cars and trucks would then rush off to deliver the liquor to individual suppliers, again for a small fee. As a result of this process, a bottle of liquor that cost \$10 in Canada might sell for \$100 or more in the United States, and the distribution of illegal alcohol made up 5% of the nation's gross national product (Schlosser, 2003). Such profits soon attracted the attention of organized crime syndicates. They took over large portions of the supply and distribution networks, although cooperation between different factions was often difficult and might be settled with gunfire¹³ (Okrent, 2010).

Prohibition had many unanticipated effects: Arguably the demand for effective alcohol sales and distribution systems, combined with the large profits to be made through this process, provided an incentive for criminal organizations to evolve (Okrent, 2010). Admittedly, territorial negotiations were aided by the judicious use of explosives or automatic weapons fire from vehicles driving past a competitor's place of business,¹⁴

but for the most part the general public ignored these activities while those who wished to do so purchased the alcohol they desired. Nor was this the only unanticipated consequence of Prohibition: Following the start of Prohibition the homicide rate in the United States increased fourfold, while other forms of crime increased by 24% (McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds, 2009). Prohibition contributed to a staggering increase in corruption among elected officials and law enforcement officers, and it also contributed to a decline in civil rights and eliminated a source of tax revenue for the government (Lessig, 2009).

At the same time, individuals who did drink switched from beer to liquor, which allowed them to achieve the highest level of intoxication in the least amount of time (Gray, 1998). When Prohibition ended, drinkers retained this pattern of alcohol consumption. In this manner, the Great Experiment helped to shape the drinking habits of people for generations to come.

Although Harry Anslinger had been promoted to the directorship of the Bureau of Narcotics, organized crime was not deterred and quickly made the transition to smuggling illicit drugs, especially heroin.¹⁵ At the same time, heroin moved out of the ghettos into middle-class America, which suddenly had to face the reality of drug addiction among their children. Since then, there have been temporary victories in which local law enforcement officials have been able to close down one avenue or another through which drugs were supplied to the consumer. Such victories have proven to be quite temporary and to have little impact on the availability of illegal drugs. The current program to interdict the flow of illicit drugs into this country has only resulted in the arrest and prosecution of individuals who used drugs or low-level drug suppliers. Occasionally a mid-level supplier is arrested and prosecuted, but such arrests are rare and the high profits associated with the distribution and sales of illicit drugs continue.

The World of Today

Today, law enforcement officials stage big media events in which they show off the piles of drugs they have intercepted. They do not mention that in spite of their best efforts, such activities only interdict an estimated 5–10% of the drugs being smuggled into the United States. To make an appreciable impact on the cost of illicit drugs, law enforcement officials would need to interdict not 5–10% but 80% of the illicit drugs being smuggled into this country (Maté, 2010). When

¹¹This is a topic that lies beyond the scope of this text.

¹²Often referred to as "rum runners."

¹³The "St. Valentine's Day Massacre" was an extreme example of how such territorial disputes were settled.

¹⁴Which sounds vaguely like the current situation between gangs selling drugs on the street corners, crack houses, and drive-by shootings, does it not?

¹⁵In one of the most ironic twists of history, Harry Anslinger would supply Senator Joseph McCarthy (1908–1957) with morphine confiscated from evidence rooms after discovering that Mr. McCarthy, whom he admired, was addicted to this compound and had been purchasing it from illicit sources (Hari, 2015).

law enforcement officials arrest an individual drug dealer or even a mid-level supplier, the high profits associated with drug smuggling and sales mean that another individual or mid-level drug dealer will step into the void to take over the sales and distribution of drugs within a matter of hours to days. Arguably, this dynamic is a legacy of Harry Anslinger. He served as an assistant to the commissioner of the U.S. Bureau of Prohibition, an agency charged with the interdiction of alcohol and the punishment of those who trafficked in it. These were goals that he wholeheartedly supported, although in retrospect they were ineffective in blocking the flow of alcohol into the country. This Prohibition-era alcohol supply and distribution system rapidly came under the control of organized crime. When he became the director of the Bureau of Narcotics, Anslinger continued to believe that the interdiction of these chemicals and prosecution of those who trafficked or even possessed small amounts for personal use was the best way to address the problem of illicit drug use.

Surprisingly, illicit drug dealers, especially those in the middle and upper levels of the supply and distribution system, would support this philosophy. It justifies their continued sale of proscribed chemicals at the price they set, making obscene profits at each level of the drug distribution system. An example of this process might be found in the efforts of law enforcement authorities in recent decades that have encouraged drug smugglers to switch from bulky, low-profit marijuana to cocaine. Pound for pound, cocaine is more lucrative to smuggle into the United States than is marijuana. An unintended side effect of the efforts at interdiction of marijuana appears to have contributed to the development of drug gangs and a wave of violence that swept across the country in the 1980s and 1990s. By arresting the older, established drug dealers, the way was opened for inner-city, violence-prone, younger drug dealers to move into the business of selling cocaine, and to fight over turf (Brust, 2004).

The Substance Use Disorders: Symptom or Disease?

Social scientists have long been aware of the strong correlation between the substance use disorders and criminal activity. Certainly, the use of such substances can result in aggressiveness, hostile behavior, and violence (Mack, 2015). However, as statistics instructors repeat to their classes, correlation does *not* imply causality. The oft-repeated statement that alcohol is associated with criminal activity illustrates this point. Alcohol is the most commonly used mood-altering chemical in society, and for that reason it would not be unreasonable to expect that a significant percentage of perpetrators were intoxicated when their crime was committed (Husak, 2004).

However, there are multiple pathways between the SUDs and criminal activity, with new substance use both arising from and predicting criminal behavior (Galaif, Newcomb, & Vargas-Carmona, 2001). Early substance misuse was found to predict later criminal activity in a community sample, according to the authors. Yet delinquency in childhood or adolescence usually *precedes* the development of substance use disorders, providing a warning sign at a stage in the adolescent's life when appropriate intervention might help reduce their risk for the later development of an SUD (Husak, 2004; Maté, 2010). Children and adolescents who develop a substance use disorder usually suffer significant physical or emotional abuse, but it is often when the individual develops an SUD that impairs impulse control and contributes to the tendency for the individual to engage in socially inappropriate behavior(s) such as theft, drug sales, or assaults that society intervenes, usually through the legal system.

Criminal Activity and Drug Misuse: Partners in a Dance, but Who Is Leading?

An age-old debate centers on the question: Which came first, the chicken or the egg? In a modified form, the same question might be applied to the SUDs: Which came first, the production of these chemicals or their use? Globally, 250 million people are thought to use illegal drugs at least once each year (United Nations, 2016), and 4 million farmers are thought to be economically dependent on the cultivation of illegal crops ("Losing tolerance with zero tolerance," 2005). In the United States, the cultivation and sale of domestically produced marijuana makes it *the* biggest cash crop in this country, and in California it brings in more money than the next five agricultural products combined ("Grass is greener," 2007; Smith, 2017). "Narco-terrorists" from various drug cartels in Mexico routinely engage in gun battles or carry out executions that have killed tens of thousands of people over the years as they fight for the money spent by Americans who desire illicit drugs (English, 2011).

Society's responses to the substance use epidemic echo the approach of Harry Anslinger to illegal alcohol use during Prohibition: Interdict supplies of illicit drugs before they reach the level of the individual users. The effectiveness of these efforts can be seen in the fact that in the last decade of the 20th century the supply and scope of drug misuse around the world *increased* rather than decreased ("Losing tolerance with zero tolerance," 2005). Further, the theory that the addict's criminal behavior is caused by his or her addiction must be discounted in the face of the fact that over 50% of opiate-dependent persons have been arrested for a criminal act(s)

before their first use of narcotics (Jaffe & Strain, 2005), and only 17% of convicted inmates reported that their criminal acts were carried out to support their addiction (Hart, 2013). These details cast doubt on the theory that drug use results in criminal acts. A counter argument is that the typical individual addicted to intravenous drugs must commit between 89 and 191 crimes a year to obtain sufficient funds to finance his or her drug use (Maté, 2010).

More than a generation ago, Elliott (1992) offered a different perspective on the relationship between the SUDs and criminal behavior. The author suggested that chemical use and criminal behavior are both a reflection of the “decline in the power of cultural restraints” (p. 599) that periodically takes place in this culture. The author supports his argument with the observation that Europe has suffered “tidal waves of crime” (p. 599) every few decades since the 14th century. A similar pattern has emerged in the United States over the past 200 years, and in each cycle there is “an erosion of personal integrity, widespread dehumanization, a contempt for life, material greed, corruption in high places, sexual promiscuity, and an increased recourse to drugs and alcohol” (p. 599, *italics added*).

Criminal Activity and Personal Responsibility

The relationship between the SUDs and criminal behavior is far more complicated than an overly simplistic drug use = crime equation (Hart, 2013). Advocates of the medical model often suggest that the SUDs reflect damage to the structure of the brain itself, pointing to neuroimaging studies that indicate that persons with SUDs have variations in the anatomy of the brain compared to those people who do not have an SUD. The question raised by such studies is whether, given these anatomical variations, the individual can be held responsible for his/her behavior (Horstman, 2010). Some would say the individual can hardly be held responsible for the anatomy of their brains, and the anatomy of the brain affects what the individual thinks. Thus, to what degree can society hold individuals responsible for their behavior if they have abnormal brains?

Another question that falls in the gray area of criminal responsibility is that between 51 and 76% of adult males and between 39 and 85% of adult females arrested for criminal activity have evidence of at least one illicit chemical in their bodies at the time of arrest (Farabee, Prendergast, & Cartier, 2002; Makki, 2003). Was their behavior prior to and after the development of the SUD a result of willful misconduct, or a reflection of an abnormal brain? If the person was under the influence of chemicals at the time of the offense, what is his or her level of responsibility? Is it the same as it would

be if he or she had not been under the influence of chemicals? The issue of personal responsibility is often sidestepped by the legal system through the assumption that drugs somehow interfered with the individual’s ability to think coherently.¹⁶ This position rests on the unproven assumption that substance use obliterates free will (Husak, 2004; Szasz, 2009). This is an extension of the “demon rum” claim often made in the 19th and early 20th centuries, which postulates that “If intoxication is wrong, it is in large part these days because it is perceived to be guilty of inciting criminality and other anti-social activities in too many of those who regularly take intoxicants” (Walton, 2002, p. 75). Note that it is the *substance* that is blamed for the criminal behavior, and not the individual. Proponents of this position believe that once the individual ingests alcohol or a drug, it overwhelms the individual’s ability to make rational choices, thus inciting the criminal behavior. In some states, a “diminished capacity” defense might be used to mitigate the full weight of the charges for offenses committed under the influence of chemicals (Gendel, 2006; Husak, 2004). However, the legal system holds that the individual is still responsible for the decision to take the initial dose of alcohol or drugs.

The decision to bring the full weight of the legal system to bear on individuals using substances demands that clear decisions be made about what is acceptable behavior for individuals in society.

[The] person to be blamed must have done something wrongful; no one can merit blame for conduct that is permissible. But whether and to what extent someone should be blamed is not simply a function of the wrongfulness of his conduct. We must also decide whether the wrongful act is fairly attributed to him, that is, whether he is responsible for it.

Husak (2004, p. 405)

If a person with an SUD acts in a manner entirely consistent with that of a person with a substance use disorder, should he or she be punished? This is a legal conundrum. To punish a person with an SUD simply because she or he has a substance use disorder violates the Eighth Amendment to the Constitution of the United States (Gendel, 2006). However, the courts have interpreted the law to the effect that a given individual should not be punished for addictive *behavior*, but then the individual is still held accountable for behaviors that are clearly part of

¹⁶So if the person tends to engage in antisocial behaviors in general, but is unable to think clearly at the time of the current arrest because he or she is under the influence of alcohol or drugs, does this exonerate him or her of responsibility for the current criminal act?

the addiction (Gendel, 2006). However, even this line of reasoning is not followed to the letter by those who prosecute drug offenders. Those persons most likely to experiment with new drugs are white, middle-class, suburban males, who tend not to believe that they can be harmed by drugs of misuse, and who have significant amounts of discretionary money at their command (Boyer, 2005). By the time a new compound has reached the inner cities, it is already a well-established drug of misuse in other social circles (Boyer, 2005). However, the focus of antidrug criminal prosecutions tends to be on social groups other than white, middle-class, suburban males.

Manufactured Criminals

The national prohibition against the use of certain compounds has resulted in a situation where users can obtain these substances only through illicit channels.¹⁷ This means that because access to these chemicals is under the control of suppliers willing to break the law in return for a rather large profit, the usual laws of a free-market economy do not apply in the illicit drug world (Reuter, 2009). However, at each level of the distribution chain, the drug suppliers demand a significant profit for their product.¹⁸ At the street level, individuals who use substances must somehow obtain the money being demanded by the dealer. To meet this price, the user must engage in either legal or illegal activities. Some persons exhaust personal finances, borrow money from family members, engage in theft, sell drugs to others for profit, or engage in prostitution (heterosexual or homosexual). Forty-one percent of females and 11% of men in the 18–29 age group who are addicted to narcotics reported being forced into unwanted sex under the threat of violence (Jessell et al., 2015).

The person who engages in theft will earn only a fraction of the stolen item's actual worth, forcing him or her to steal even more to obtain the desired funds. It has been estimated that the typical heroin addict needed to steal \$200,000 worth of material each year to support their addiction (Kreek, 1997). It can thus be argued that the national prohibition against the use of heroin (or other drugs, since a similar process exists for the other compounds deemed illegal) contributed to the wave of crime that swept across the country in the latter half of the 20th century.

¹⁷An exception to this rule are those individuals who have prescriptions for controlled substances, such as patients who receive prescriptions for narcotic analgesics to control pain.

¹⁸Hari (2015) estimated that the profits for the drug cartels just in Mexico are between \$19 and \$29 billion a year.

Drug Use and Violence: The Unseen Connection

Violent crime is estimated to consume 11.9% of the Gross National Product of the United States each year (Schiffer et al., 2011).¹⁹ Brust (2004) identified three categories of substance-related violence: (1) *pharmacological violence*, or drug-induced violent behavior; (2) *economic compulsive violence*, or violent crimes committed by a person to obtain money necessary to purchase illicit compounds; and (3) *systemic violence*, or the violence that is associated with the illicit drug distribution network. Collectively, these forms of violent behavior account for three-quarters of the homicides committed each year in the United States (Hari, 2015).²⁰

The most commonly misused chemical, alcohol, provides an excellent example of pharmacological violence. Approximately 50% of all sexual assaults, for example, are committed by men who have ingested alcohol (Abbey, Zawacki, Buck, Clinton, & McAuslan, 2001). While one might argue that the disinhibition effects of alcohol might entice individuals to carry out a sexual assault, the use of “date rape” compounds would argue that such an act was premeditated rather than spontaneous, as the user must first obtain the compound and then choose the most advantageous time to slip it into the victim's drink, both planned activities. Most certainly those who use such compounds engage in a degree of prior planning, but at what point does an impulsive act become a premeditated act?

The effects of the amphetamines and cocaine also provide excellent examples of pharmacological violence, since both compounds predispose the user toward violence, both against others and against the self. Individuals who use cocaine, for example, were more likely to die from homicide or suicide than were age-matched control subjects (Gold & Jacobs, 2005). There are many reasons for this: First, the lifestyle forced on those persons who use these compounds brings them into frequent contact with people who are more likely to respond with violence, either because of their premorbid personality or because of pharmacologically enhanced violent tendencies. Also, the behavior of a person under the influence of cocaine or the amphetamines might induce others to respond with violence, possibly resulting in a “victim-precipitated homicide.”

¹⁹For example, the lost productivity due to violent crime, medical treatment of those who survive their brush with violence, burial expenses for those who do not, the cost for law enforcement personnel to apprehend and incarcerate violent offenders, the costs of the judicial system as the case slowly winds its way through the courts, and, if convicted, the costs associated with incarceration of a violent offender, plus parole supervision upon release.

²⁰Hari (2015) offered an excellent example: When a major drug supplier is arrested or killed, there is a power vacuum that others will seek to exploit, sometimes through violent means.

Additionally, women who admitted to the recent use of heroin were 2.7 times more likely to suffer a physical injury as a result of interpersonal violence in the next 6 months (Gilbert, El-Bassel, Chang, Wu, & Roy, 2011). Women who were the victims of sexual violence were more likely to resort to amphetamine or cocaine use after the assault (Gilbert et al., 2011). The authors suggested that the hospital emergency department setting provided a milieu for brief intervention and treatment referrals for victims of interpersonal violence, with the anticipated result of future reduced morbidity and mortality for victims of interpersonal violence.

Earlier in this chapter, it was noted that the disinhibition effect of alcohol contributes to many sexual assaults each year in this country. It is not unreasonable to assume that the same mechanism might be involved in many homicides that take place each year in the United States. This is not to say that alcohol use *caused* the individual to commit the homicide in every case. Rather, a significant percentage of homicides were apparently planned in advance, and then the perpetrator(s) consumed alcohol to bolster their courage before committing the act. In other cases, the homicide is an unplanned act brought on during the heat of passion, in which the individual's self-control was reduced through his or her use of alcohol.

A common cause of substance-related death is criminal attack by drug dealers, other addicted persons, or individuals looking for vulnerable persons to prey upon. Drug dealers have been known to attack customers, safe in the knowledge that the victim is unlikely to go to the police to report a criminal attack when the victim was also involved in criminal activity (drug use itself, or the various activities that the addicted person must engage in to support their addiction). Kleiman (2011) observed that "In an illicit market, the level of violence and the share of the revenue available to those who use it, rises along with the level of [law] enforcement" (p. 124). This is consistent with the fact that drug dealers have been known to kill clients for unpaid drug debts and as a warning to others who might also owe the dealer money.²¹ They have also been known to kill bothersome clients by selling them a bag of exceptionally potent drugs so that the client will die of an overdose. Individuals addicted to drugs have also been known to kill drug dealers, although the frequency with which such assaults are premeditated is not known at this time. Rival drug dealers have been known to engage in gun battles over "turf,"²² and drug dealers have been dumped

in front of a hospital emergency room by a rival, who speeds off before the police arrive. Sometimes the victim will live, but it is unlikely that she or he will provide the police with any useful information, so as to avoid self-incrimination.²³

Schiffer and colleagues (2011) utilized brain-imaging technology to examine the brains of violent offenders as opposed to those who simply use substances, as well as a sample of control participants. The authors found that violent offenders tended to have a higher concentration of neurons (the gray matter of the brain) in the mesolimbic reward system of the brain, suggesting that for these persons the reward system is more easily activated.²⁴ Persons with substance use disorders demonstrated subtle anatomical differences in the form of reduced numbers of neurons in such areas of the brain as the orbitofrontal complex, suggesting that for this group violence might be a result of reduced inhibitions rather than increased pleasure in violent behaviors.

Partner-Associated Violence

There is a known relationship between substance use disorders and violence between relationship partners. However, violence at the hands of a relationship partner is often multifaceted (Smith, Homish, Leonard, & Cornelius, 2012). The *reason* for the violence varies from case to case, and there is a need for systematic research into this topic. Many drugs lower inhibitions, including those inhibitions that help to control anger, contributing to partner-associated violence. In other situations, both relationship partners might be under the influence of chemicals at the time of the violent outburst(s), possibly contributing to one or both individuals engaging in violence-precipitating behaviors that normally would be out of character for them.²⁵ The violence might ensue following verbal altercations between partners over the diversion of financial resources to fund substance use by one or both individuals, confrontation by one partner about how the other is not living up to financial, emotional, or parental duties, or over the allocation of substances to be misused.

Following the violence, the victim—and often the perpetrator, who might feel remorse for their behavior—turns to drugs for solace. Smith and colleagues (2012) noted, for

²¹One popular method used by cocaine dealers who wish to kill a bothersome client is to sell the addict the powdered residue of car battery acid that accumulates on the battery terminals, possibly mixed with cocaine, which then will kill the individual. This is often referred to as a "hot shot."

²²Usually a street corner on which to sell drugs, although on occasion the right to sell drugs in a certain part of the community.

²³Well officer, I was just standing on the street corner, minding my own business and selling the occasional bag of heroin, when this guy pulls up in a car and shoots me so that he can sell heroin from that street corner!" This is a discussion that is quite unlikely to take place, is it not?

²⁴Which is consistent with the comment made by many sociopaths that they simply *like* to fight.

²⁵Such as one partner slapping the face of the enraged partner who was holding a weapon, or verbally encouraging the enraged partner to use the weapon ("come on, you're too much a coward to use that!" for example, with unfortunate results).

example, that women who were the victims of interpersonal violence often misused alcohol and narcotic analgesic medications, but only rarely engaged in the misuse of other compounds. Men who were the victims of interpersonal violence were found by the authors to misuse narcotic analgesics as well as other drugs of misuse, but only rarely alcohol (Smith et al., 2012). This attempt at self-medication might then contribute to increased vulnerability of the victim. There is a relationship between partner-associated violence and post-traumatic stress disorder,²⁶ a common consequence of partner-associated violence, which might further contribute to the misuse of chemicals by the victim, who seeks escape from the painful symptoms of this condition. This is only a theory, but it does seem to account for the observed relationship between partner-associated violence and substance misuse.

Adulterants

Unless the drug being sold is a pharmaceutical that was diverted to the illicit drug market, it is rare for drugs to be sold to the individual who uses drugs in their pure form (“Deadly drug adulterants,” 2008; Isaacs, Harper, & Miller, 2017). More commonly, the compound sold to the individual drug user has been highly adulterated, possibly to the point that has been estimated that between 75 and 90% of the cost of cocaine or heroin at the street level is the result of adulteration after the product reaches this country (Kleiman, 2011). On occasion the compound sold might not even be the compound that it is supposed to be at the time of the sale!²⁷ The upper-level drug dealer might buy a kilogram of cocaine, combine it with mannitol, and sell the two kilograms of resulting powder to a lower-level drug dealer, doubling his or her profits (“Deadly drug adulterants,” 2008). If the drug must pass through four or five levels of distributors, each of whom also adulterates the compound by 50% to increase profits, the final product will be one that is quite diluted. Surprisingly, one strong supporter of drug adulteration was Harry Anslinger, who thought that drug adulteration would discourage people from using drugs (Hari, 2015).

The financial incentive for adding an adulterant to an illicit drug at each level of the supply chain is clearly demonstrated by the fact that “It costs approximately \$300 to

purchase enough coca leaves to produce a kilogram of cocaine, which retails for about \$100,000 in the United States when sold in one-gram, two-thirds pure units [of cocaine]” (Reuter, 2009, p. 50). If the “cocaine” is further adulterated so that each individual gram was only 50% cocaine, the profit margin for the dealer would be further inflated. Since the sale of illegal drugs is not carried out in a free market where customers can compare prices and shop for the least expensive price for the desired compound, the customer pays whatever they are told to pay by the dealer. Levamisole®, a compound once used by physicians in the United States to treat roundworm infection (and which is still used in veterinary medicine for that purpose) is one common adulterant (Zhu, LeGatt, & Turner, 2009). Approximately one-third of the cocaine samples tested were found to contain Levamisole, which in rare cases is capable of inducing the blood disorder known as agranulocytosis.²⁸

Another example of this process is found in the illicit narcotics production and distribution process: The opium farmer might be paid \$90 for a kilogram of raw opium, which is then adulterated at each step of the distribution process, increasing profits by as much as 1,600 times by the time when the drug reaches the individual intending to use the substance (Schuckit, 2006a, 2006b). Street samples of illicit heroin in the United States have been found to range from 18 to 71% pure heroin (“How they smack up,” 2005), which means that adulterants make up 31–82% of each sample sold on the streets. Common adulterants in heroin include substances such as lactose, acetaminophen, and fentanyl, which is at times 50% more potent than heroin (Isaacs et al., 2017). This is consistent with the dictum that product reliability and safety are hardly priorities for those who traffic in illegal substances. Deception is common and compounds are often misrepresented. For example, less than 50% of the MDMA tablets sold actually contained that compound, with compounds such as caffeine, aspirin, cocaine, PCP, LSD, narcotics, GHB, ketamine, dextromethorphan, and paramethoxyamphetamine (PMA) being sold under the guise of MDMA (Grob & Poland, 2005; Simek, 2015).

One rarely considered aspect of drug adulteration is that these compounds have the potential to do damage to the individual's body and emotional state independent of the drug(s) being used. A person who unknowingly smokes low-grade marijuana that has been intermixed with PCP to make it seem more powerful might suffer significant psychiatric harm if they have little or no experience with the effects of phencyclidine, for example. If the illicit drug

²⁶Discussed in Chapter 25.

²⁷Simek (2015) cited one study conducted in New York City that found that only 13% of the samples of “MDMA” examined contained even a trace of that compound. Other samples of purported MDMA were found to contain cocaine, amphetamine, Sudafed®, and heroin, either alone or combined with other compounds.

²⁸The nature of this disorder lies outside of the scope of this text, and interested readers are referred to the appropriate medical textbooks.

is used intravenously, the adulterants are injected directly into the individual's body, bypassing the defensive acids and enzymes of the digestive tract (Leavitt, 2003). Popular belief suggests that drug dealers will mix deadly compounds in with the drug(s) being sold, although this is rarely done since it would (a) kill off the dealer's customer base, (b) thus be bad for business, and (c) give that drug dealer a bad reputation in a market where word-of-mouth advertising is the only form of advertising that exists ("Deadly drug adulterants," 2008). However, this does seem to be taking place, considering the increase in deaths due to fentanyl (Isaacs et al., 2017). Sometimes by accident and other times by design, deadly adulterants are sometimes included in the mixture.

Identified adulterants fall into one of five categories: (1) various forms of sugar, (2) stimulants, (3) local anesthetics, (4) toxins, and (5) any of a wide range of inert compounds that can be added to give the product bulk. Some of the compounds found in samples of illicit "drugs" include mannitol, lactose, glucose, caffeine, lidocaine, acetaminophen, diphenhydramine, quinine, and even on occasion heroin in substances that were not sold as heroin, and fentanyl in substances sold as heroin²⁹ (Gold & Jacobs, 2005; Isaacs et al., 2017). Marijuana is frequently adulterated, and it is not uncommon for up to half of the "marijuana" purchased to be seeds and woody stems that must be removed before it can be smoked. Low-potency marijuana has been known to be laced with other compounds such as Raid® insect spray, PCP, cocaine paste, dry cow manure,³⁰ alfalfa, apple leaves, catnip, cigarette tobacco, hay, licorice, mescaline, opium, wax, and wood shavings.

Samples of marijuana sold have been found to have been sprayed with an herbicide such as paraquat. Two compounds found in samples of marijuana recently purchased in Europe are homosildenafil (HS) and thiohomosildenafil (THS), compounds whose effects are very similar to that of the sildenafil family of compounds, which is sold in the United States as treatment for erectile dysfunction ("Cannabis booster," 2008). Authorities are not sure whether these compounds have been added to the marijuana to enhance the absorption of the psychoactive compounds in the smoke, or to enhance the reputed aphrodisiac effect of marijuana. Unfortunately, scientists do not know how these compounds will affect the human body if smoked, since this is not the usual method of administration for the sildenafil compounds ("Cannabis booster," 2008).

²⁹Which can be a problem if you did not know that the product you had purchased contained heroin and/or fentanyl, since this could lead to a potentially fatal overdose.

³⁰Which may expose the user to salmonella bacteria.

TABLE 37-1 Known Adulterants in Illicit Drugs

Illicit Cocaine: Known Adulterants	Illicit PCP: Known Adulterants	Illicit Heroin: Known Adulterants
Acetaminophen	Ammonium chloride	Acetaminophen
Aminopyrine	Benzocaine	Acetone
Ascorbic acid	Caffeine	Acetylcodeine
Aspirin	Ketamine™	Arsenic
Benzene	Magnesium sulfate	Caffeine
Benzocaine	Procaine	Diazepam
Boric acid	Toluene	Ethanol
Caffeine		Fentanyl
Corn starch		Lidocaine
Dextrose		Methaqualone
Diphenhydramine		Phenobarbital
Ephedrine		Quinine
Fentanyl		Strychnine
Heroin		Thebaine
Inositol		Toluene
Lactose		Vitamin C
Levamisole		
Lidocaine		
Mannitol		
Methaqualone		
Niacinamide		
Phenacetin		
Phentermine		
Phenylpropanolamine		
Procaine		
Quinine		
Sucrose		
Tetracaine		

SOURCE: Karch (2009); Roth, Benowitz, and Olson (2007).

A partial list of the compounds found to be mixed with illicit cocaine samples can be found in Table 37-1. This is only a partial list, and new adulterants are being identified almost daily. As this list illustrates, however, when it comes to the world of illicit drugs, let the buyer beware!

Because of the problem of adulterants, individuals who use drugs often prize pharmaceutical agents. These compounds are of known potency, and are unlikely to be contaminated. However, they are still mixed with “fillers” that help to give the tablet or capsule shape and form. When an individual takes a compound orally, the digestive juices help to break down these inert compounds intermixed with the pharmaceuticals. For example, methylphenidate tablets are mixed with talc, which helps to give the tablet form. When crushed and injected, the talc in the methylphenidate tablet is injected into the body as well, forming micro-emboli in the circulation which might potentially damage organs such as the heart, eyes, lungs, and brain (Greenhill, 2006). The same phenomenon is found when an illicit drug is used: The adulterants may be introduced into the body, with unknown consequences. In many cases the adulterants cause local irritation to the tissue(s) into which it was injected, which then establishes the potential for an infection as the body’s defenses break down at the site of injection.

The subject of adulterants is worthy of a book in its own right, for the various adulterants can damage virtually every organ in the body.

“Designer” Drugs

When a pharmaceutical company develops a new drug, it applies for a patent on that compound. This process requires, in part, that the chemists for the company identify the exact chemical structure of that drug molecule. After review by the Food and Drug Administration, the pharmaceutical company might be granted a patent of that specific drug molecule. Unfortunately, because of the internet, production methods for illicit compounds are disseminated virtually instantly, and “legitimate chemical research can be hijacked by anyone with a hot plate and an Internet connection” (Piore, 2012, p. 43). The goal of this process is to find an “almost-like” compound that has not yet been classified as a controlled substance by law enforcement agencies. That chemical might then be sold without fear of criminal prosecution, at least until law enforcement agencies are able to have that drug molecule banned. Certainly, this is an ongoing process, as new substances are reviewed on a regular basis, such as the 12 substances (10 of which have been brought under international control) that were reviewed by the WHO Expert Committee on Drug Dependence (ECDD) in 2016, as well as the eight that were reviewed in 2015 (seven of which were brought under international control). Although creating *drug analogs* is not a new process, the creation of new designer drugs has sped up in recent years, with no indication of slowing (Connor, Feeney, Kelly, & Saunders, 2016).

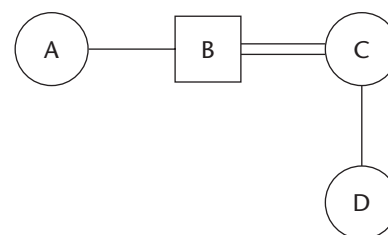


FIGURE 37-1 Parent “Molecule.”

Since drug molecules are complex structures involving hundreds of atoms, it might be possible to develop dozens, or scores, of variations on the “parent” drug. Many of these compounds are then sold in the hope that one will become the latest craze and thus make the drug distributor rich. These compounds are called “designer” drugs, some of which are less potent than the original parent drug. However, some designer drugs are just as potent as the original drug, while some are even more potent than the parent. All it takes is for a chemist to alter the chemical structure parent drug molecule, possibly by as little as one atom.

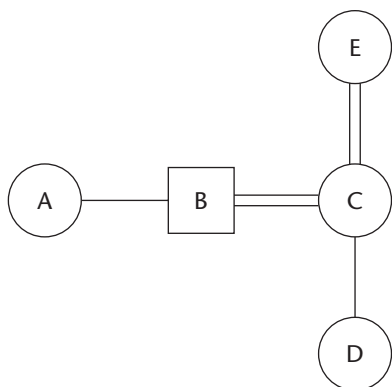
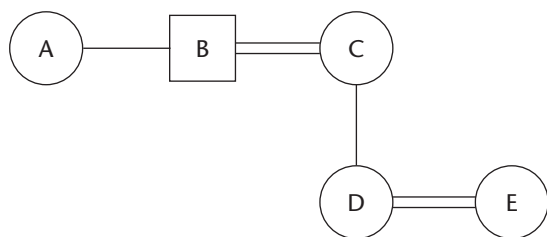
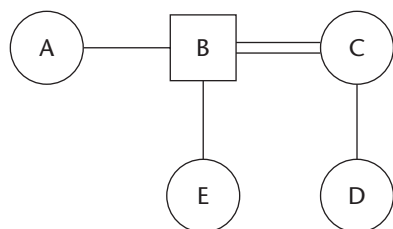
To illustrate this process, assume that the illustration in Figure 37-1 is that of an illicit drug “molecule” of a hallucinogenic compound.³¹ Admittedly, the molecule used to illustrate the process of making designer drugs has only four atoms, as opposed to the thousands of atoms found in actual drug molecules, but it does serve to illustrate the process.

To create more demand, and possibly avoid criminal prosecution if the new variant has not yet been deemed illegal, the chemical structure of the original parent compound might be altered, possibly by adding just a single atom. Technically, this addition makes this a “different” drug, since the molecular structure is not exactly the same as that of the parent compound (see Figure 37-2).³²

The new compound is called an *analog* of the parent compound. It might be as potent as the original compound, but because of the altered chemical structure it might not have been deemed illegal yet. The Food and Drug Administration does have the power to declare drug analogs illegal until a formal law can be passed, but to do so it is necessary for their chemists to identify the exact chemical structure of the analog. When this happens, it would be a simple matter to alter the chemical structure of the analog to build a new designer drug, starting the process over again. See Figure 37-3.

³¹The author understands that these are not representations of actual molecules, but he has simplified the process for many readers.

³²Simek (2015) gave the example of when criminal charges against a man in Dallas were dismissed because the police misspelled the chemical name of the compound by a single letter. This meant that the chemical for which the man had on his person when he was arrested was not the chemical that he was charged with possessing when he appeared in court, and charges had to be dropped.

**FIGURE 37-2** First Analog.**FIGURE 37-3** Second Analog.**FIGURE 37-4** Third Analog.

The change might be very subtle, and either to escape criminal prosecution or to increase profits by creating a new product that illicit drug distributors are willing to provide for a very high price, the chemical structure of the compound might be altered yet again. See Figure 37-4.

Although the “drug” molecule used to illustrate this process is a very simple one, it does serve to illustrate how it is possible to produce analogs of an original compound. In the case of real drug molecules, there might be dozens, even hundreds of possible analogs. Further, the speed with which illicit drug chemists carry out this process might be seen in the fact that by the time that the recreational substance mephedrone was classified as an illegal substance in England, new substitutes that had yet to be banned were being sold (“Ban later, ask questions first,” 2010). In the next section, we will examine some of those drug analogs that have been identified by law enforcement agencies over the years.

Some Existing Drug Analogs

Amphetamine-Like Designer Drugs

The amphetamine molecule lends itself to experimentation, and several analogs of the parent amphetamine molecule have been identified to date. One is 2,5-dimethoxy-4-methylamphetamine, or the hallucinogen DOM (also known as STP), which is rarely used by those who use illicit drugs currently. The compound MDMA (“ecstasy”) is considered an analog of the amphetamines by some pharmacologists, and there are 184 known analogs of the MDMA molecule, some of which are known to have a psychoactive effect on the user. For example, the compound 3,4-methylenedioxymphetamine, or MDEA (also referred to as MDE or MDA), has a chemical structure that is very similar to that of MDMA and has very similar effects on the user. This substance is often sold under the name of “Eve.” There are many additional similar amphetamine-like drugs, some of which have recently been deemed illegal, such as para-methoxymethylamphetamine (PMMA), which is sometimes called “red Mitsubishi” (World Health Organization, 2016g).

Another designer drug is known as “ya ba” (“crazy medicine” in Thai language). It is most commonly used in Southeast Asia (Hilditch, 2000; Kurutz, 2003) and is especially problematic in places like Bangladesh at present (Jamal et al., 2016). This compound is a blend of ephedrine, caffeine, methamphetamine, lithium (obtained from batteries), and some other chemicals obtained from household cleaning agents. It provides an 8–12 hour high, and can be inhaled, smoked, or used through a transdermal patch, but the preferred method of misuse is orally. Long-term use appears to contribute to suicidal or homicidal thoughts,³³ and most individuals follow a pattern of using the compound for 2–3 days followed by a day or two of deep sleep. Very little is known about the toxicology of ya ba, which has not been subjected to clinical research studies by pharmacologists.

Khat

In the 1990s, it was feared that methcathinone (“kat,” “quat,” or “khat,” also known as “miraa” in some areas) might become the next popular drug of misuse in the United States. Khat leaves have been chewed for centuries where the leaves are indigenous, for the psychoactive properties from the naturally occurring cathinone in the plant (Rech, Donahey, Cappiello Dziedzic, Oh, & Greenhalgh, 2015). Khat is rarely misused except among some immigrants from sub-Saharan Africa who continue the practice of chewing the leaves for their

³³Thus, this compound’s name.

psychoactive effect (Karch, 2009; “Khat calls,” 2004). On the other hand, it is of growing concern in synthetic forms, as illicit chemists have produced at least 30 variants with numerous street names to refer to what are usually called synthetic cathinones or “bath salts” (Rech et al., 2015). This is another example of drug users attempting to circumvent the prohibition against cathinone. These drugs are sold to individuals who use illicit drugs as a “safe” alternative to ecstasy,³⁴ despite the overdose risk and numerous side effects (Rech et al., 2015). These variants are sold in a variety of places, such as convenience stores and smoke shops.

WHERE KHAT IS OBTAINED

Khat is naturally found in several parts of the world, including East Africa and southern Arabia (Haroz & Greenberg, 2005; Virani, Bezchlibnyk-Butler, & Jeffries, 2009). In the natural world, the plant grows to between 10 and 20 feet in height, and the leaves produce the alkaloids cathinone and cathine. Illicit drug manufacturers began to produce an analog of cathinone³⁵ known as methcathinone, which has a chemical structure very similar to that of the amphetamines and ephedrine (Karch, 2009). It was then made available to individuals in the United States. Chemists have identified at least 20 variations of the basic cathinone molecule being sold on the illicit drug market (United Nations, 2016).

THE LEGAL STATUS OF KHAT AND SYNTHETIC CATHINONES

Khat was classified as a Schedule I compound in 1992, and its manufacture or possession are illegal in the United States. However, cathine is easily manufactured in illicit laboratories by chemically transforming the ephedrine molecule by adding an oxygen atom to it using such products as drain cleaner, epsom salts, battery acid, acetone, toluene, and various dyes. The end product is a compound with the chemical structure 2-methylamino-1-phenylpropan-1-one, which is then sold to illicit drug users. Since they were sold as bath salts and were labeled as not intended for internal consumption, their sale was technically legal. Such products have been reviewed by the Food and Drug Administration and, in many cases, have been placed on the controlled substances list by the DEA.

METHODS OF KHAT AND SYNTHETIC CATHINONE ADMINISTRATION AND EFFECTS OF THIS COMPOUND

Individuals typically smoke khat, although it can be injected. On rare occasions the leaves are also chewed. The effects of khat are very similar to those of the amphetamines. This is understandable since the khat plant contains norephedrine and cathinone, which is biotransformed into norephedrine

in the body following ingestion. Like the amphetamines, khat can induce dopamine release and a sense of euphoria, excitement, grandiosity, increased blood pressure, and flushing of the skin (Virani et al., 2009). There are reports that the effects last in excess of 24 hours, although more reputable sources suggest that the effects last 3–4 hours. However, methamphetamine is easier to manufacture, and so khat never became a popular drug of misuse in the United States. Synthetic cathinones are often snorted or taken orally, although a variety of other methods are used (such as “bombing,” which is wrapping the substance in cigarette paper to then swallowing it) (Rech et al., 2015).

ADVERSE EFFECTS OF KHAT

There has been little research into the actions of khat or synthetic cathinones on the body. What little is known is drawn from clinical data from physicians who have treated patients who have used this compound. Known adverse effects of khat include vasoconstriction, hyperthermia, hypertension, insomnia, anorexia, constipation, drug-induced psychosis, hallucinations, paranoia, aggressive episodes, anxiety, cardiac arrhythmias, mood swings, depression, tremors, seizures, and even death (Haroz & Greenberg, 2005; Rech et al., 2015). Following extended periods of use, it is not uncommon for the individual to fall into an extended period of sleep that might last days.

There is preliminary evidence suggesting that khat is capable of inducing a syndrome similar to Parkinson’s disease (“Parkinson-like symptoms linked to illicit khat use,” 2008). In one of the few studies to be published in this area, Stephens and colleagues (2008) drew on clinical evidence from 23 adult intravenous khat addicts from Latvia, where khat misuse is common. The research participants had an average period of injected khat use of 6.7 years, and their average age was 37.5 years. It was noted that a gait disturbance predated the development of other symptoms, and there were no psychiatric problems noted in the research sample. Unfortunately, it was discovered that even if patients discontinued the use of khat, there was no improvement in their neuropsychiatric status, suggesting that the damage to the brain is permanent (Stephens et al., 2008).

Mephedrone

This compound is a synthetic analog of cathinone, and as such is thought to have the same CNS stimulant effects (Fleming, 2010). Although it was first synthesized in 1929, those who use illicit drugs did not discover it until around 2003. It was not a controlled substance at the time, and little is known about the effects of mephedrone and related compounds in the body. There has been a great deal of media attention devoted to mephedrone, much of it based on hearsay

³⁴Discussed in Chapter 12.

³⁵Known in Europe by the name of *ephedrone*.

or secondhand knowledge (Owen, 2013).³⁶ As of this time it has been classified as illegal in at least 13 countries (Fleming, 2010), including the United States, which classified it as an illegal substance in July of 2012.

There has been virtually no research into the pharmacokinetics of this compound, and what is known is based on case reports of persons who have used these compounds. Effects following oral use of mephedrone peak after about 2 hours if taken on an empty stomach. Food will delay absorption of the mephedrone, but eventually it is all absorbed by the body. When snorted it will begin to take effect in about 30 minutes. The effective dose for snorted mephedrone is lower than when ingested. Rectal insertion of the compound into the body³⁷ also requires a lower dose to achieve the desired effects. Mephedrone's desired effects appear to be very similar to those of MDMA: a sense of empathy and closeness with others, possible sexual arousal, and CNS stimulant effects such as those seen when a person has ingested MDMA. Some of the reported side effects of mephedrone include anxiety, tachycardia, hypertension, nose bleeds, sweating, piloerection, nausea, and vomiting. There have been case reports of deaths subsequent to mephedrone use in both the United States and Europe (Maskell, De Paoli, Seneviratne, & Pounder, 2011). There has also been one isolated case of mephedrone-induced delirium, and one case resulting in subsequent death from cardiac arrest (Lusthof et al., 2011).

MDPV (3,4-Methylenedioxypyrovalerone)

This is a chemical relative of mephedrone and was also sold "bath salts," either in isolation or mixed with mephedrone. The bags containing the bath salts were labeled "not for human consumption" and thus it was not an illegal compound at first. There has been little systematic research into MDPV's toxicology, and much of what is known about its effects is based on clinical case reviews. It first emerged as a misused compound around 2004 and has been increasing in popularity since then (Leo & Goel, 2012). MDPV powder can be snorted, ingested orally, or inserted rectally, and will produce effects very similar to those induced by cocaine, methylphenidate, or dextroamphetamine (Leo & Goel, 2012). Individuals using this substance report feeling more alert, less

need for sleep, and a sense of euphoria. As the dose and duration of use increase, the individual is more likely to experience the negative effects of MDPV, which include increased blood pressure, tachycardia, peripheral **vasoconstriction**,³⁸ anxiety, irritability, agitation, panic, psychosis, and delirium (Leo & Goel, 2012). While the desired effects seem to last 3–4 hours, MDPV's ability to cause tachycardia and hypertension seems to last about 6–8 hours after it is used. This compound was classified as an illegal compound by the Drug Enforcement Administration in July of 2012.

THC-Like Designer Drugs

In recent years, a compound sold as "synthetic marijuana" appeared on the market, and its use has now spread around the world. Local names for this compound include (but are not limited to) "K-2" and "spice." These compounds are usually produced by clandestine laboratories, and their use has become a worldwide phenomenon, in part because they cannot be detected by traditional urine toxicology tests (Castaneto et al., 2014). Hundreds of THC analogs have been isolated, all of which are more potent than THC itself (Rech et al., 2015). One of these THC analogs is HU-210, which was first synthesized at the Hebrew University in 1988 by chemists who were searching for a compound that would help treat depression (Barth, 2012). It was not long before individuals who use illicit drugs discovered that synthetic cannabinoids bind at the CB1 receptor site 2–100 times more strongly than does THC, which, as discussed in Chapter 10, itself binds at the cannabinoid receptor sites more strongly than do the endogenous cannabinoids (Barth, 2012; Castaneto et al., 2014).

Preliminary research into some of these THC analogs suggests that they have the potential to function as potent anti-inflammatory compounds, while other studies suggest that they might inhibit the growth of malignant tumors, control seizures, and possibly function as a new class of analgesics. However, these are controlled laboratory studies involving highly purified compounds obtained from marijuana. Many THC analogs are being used for their ability to allow the individual to become high. They were originally legally produced in the United States, sometimes as a form of incense, and the packets were marked "not for human consumption," circumventing the drug control laws.

The dosage levels being used are potentially toxic to the individual, and a number of people have been hospitalized after using a THC analog. Acute adverse effects of synthetic cannabinoids include nausea, vomiting, respiratory problems, hypertension, ischemic stroke, damage to

³⁶Owen (2013) offered as evidence the story that the "Miami zombie," who was confronted by police after biting off a piece of another person's face and who was ultimately shot by the authorities. The news media reported that he was under the influence of "bath salts," and this story was repeated time after time. Unfortunately, extensive toxicology testing failed to detect any evidence of mephedrone or other components of bath salts, although the results from these tests were not available when the initial news reports were issued.

³⁷Sorry, you will have to use your imagination on this one!

³⁸See Glossary.

the kidney, chest pain, heart attacks, tachycardia, anxiety, agitation, paranoid psychosis, insomnia, seizures, and suicidal ideation (Castaneto et al., 2014; Furek, 2011; Mir, Obafemi, Young, & Kane, 2011; Murphy et al., 2013). There is evidence of cognitive impairment as a result of THC analog use; however, it is not known whether this is a temporary or permanent effect of use. The long-term adverse effects of these compounds are unknown since research into the toxicology of these compounds has not been completed at this time. In 2015, an alert was posted by NIH concerning an increase in overdoses related to these compounds. Many of the known THC analogs have been declared illegal by the Drug Enforcement Administration, but illicit drug chemists have proven adept at developing new synthetic cannabinoids that have not been classified as illegal substances.

Hallucinogenic Designer Drugs

PCP is a popular drug molecule for illicit chemists to experiment with, and there have been at least 30 drug analogs of PCP identified to date. Some of these compounds are more potent than PCP, such as the compound N-ethyl-1-phenylcyclohexylamine (also known as PCE), or the compound 1-(1-1-thienylcyclohexyl) piperidine (TCP). Other drug analogs of PCP are 1-(1-phenylcyclohexyl)-pyrrolidine (PHP), 1-piperidinocyclohexanecarbonitrile (PCC), as well as 3-methoxy PCP (3-MeO-PCP) and 4-methoxy PCP (4-MeO-PCP). These complex chemical names provide some idea of how the PCP parent molecule might be manipulated by chemists to develop other compounds.

KETAMINE³⁹

Ketamine is a chemical that is in a gray area of medicine at this time: It is used by physicians in special circumstances, but it is also a popular drug of misuse. The chemical structure of ketamine is similar to that of PCP and is used by physicians as a surgical anesthetic that does not cause the respiratory or cardiac depression caused by other anesthetics (McDowell, 2005; Schultz, 2002), as well as by physicians in the emergency room treating agitated patients (Hopper et al., 2015). It is also used by trauma surgeons in combat zones to reduce pain levels. Early experimental evidence suggested that it is effective in the treatment of depression, especially depression that has been resistant to other treatments, often inducing remission depression in just a few hours (Chaki, 2017). However, current research suggests that the misuse potential, dissociative symptomology, and other problems make it not useful for general treatment (Chaki, 2017).

³⁹Or 2-(2-chlorophenyl)-2-(methylamino)cyclohexanone, if you really must know.

Ketamine has been classified as a Schedule III compound⁴⁰ since 1999. It has a fairly wide therapeutic window, and thus is relatively safe when used as directed in a medical setting. It does have a shorter duration of action than PCP, with peak blood levels being seen approximately 20 minutes after it is ingested by mouth. When it is used as an anesthetic and is injected into a vein, its effects are seen with seconds (Sadock, Sadock, & Ruiz, 2015).

In the brain, Ketamine binds at the NMDA receptor site, forcing a calcium ion channel to close (McDowell, 2004, 2005). This slows the rate at which the neuron can fire. The elimination half-life of ketamine is 3–4 hours, and it is extensively biotransformed by the liver before elimination. Only about 3% of a single dose is excreted unchanged in the urine. Standard toxicology tests will not detect ketamine, and so if a date rape situation is suspected, a special toxicology test must be ordered to detect the drug or its metabolites. Analgesia induced by a single injection of ketamine begins in about 60 seconds when injected into a vein and lasts about 40 minutes, although the patient might experience a dissociative state that lasts for hours after it is used (Sadock et al., 2015; Virani et al., 2009). During this dissociative state, the individual will have trouble forming memories, which makes this medication of value during the acute recovery stage following surgery. A common complication when it is used as a surgical anesthetic is a lack of concern for the environment or personal safety (Sadock et al., 2015).

It is possible to manufacture ketamine in illicit laboratories, but it is rather difficult to do this, and most commonly the ketamine found on the streets is diverted, usually from veterinary supply companies since it is used for surgery with animals (McDowell, 2005; Sadock et al., 2015). It is a colorless and odorless compound, and can be misused by intranasal, oral, inhalation,⁴¹ or on rare occasions intravenous injection (Sadock et al., 2015). In powdered form, it might be intermixed with tobacco or marijuana and then smoked (Gahlinger, 2004). The fact that it is odorless and colorless makes it an ideal date rape drug, since it can be slipped into the victim's drink without arousing suspicion, while its ability to induce **anterograde amnesia**⁴² will reduce the chance that the rapist will be identified by the victim.

The most common group of individuals who misuse ketamine are 18–25-year-old adults (Lewis, 2011), who take advantage of the fact that the effects of an oral dose of ketamine are dose-dependent (Freese, Miotto, & Reback, 2002; Gahlinger, 2004). Dosage levels typically used are about one-half of that necessary to induce anesthesia,

⁴⁰See Appendix 3.

⁴¹This is referred to as a “bump” by those who use this method.

⁴²See Glossary.

or about one-sixtieth of the LD50 for this compound (McDowell, 2004, 2005). Such dosage levels induce a sense of euphoria, visual hallucinations, a dissociative state, and vivid dreams (Freese et al., 2002; Gahlinger, 2004). Other effects of ketamine when it is used include (Gahlinger, 2004; McDowell, 2004, 2005; Sadock et al., 2015; Walton, 2002) hypertension, tachycardia, respiratory depression, paranoia, apnea, anxiety, and flashback experiences in the days or weeks after the last use of this compound. Long-term misuse can induce memory problems (Gahlinger, 2004; Morgan, Muetzelfeldt, & Curran, 2009). Individuals who use ketamine frequently experience deficits in the areas of spatial memory and pattern recognition on psychological tests, as well as delusional thought patterns that appear to resolve with abstinence (Morgan et al., 2009). Those who use ketamine long-term run the risk of bladder shrinkage, urinary incontinence, and damage to the kidneys and ureter (Bhattacharya, 2011).

AMINOEX⁴³

This compound was introduced in Europe as an aid to weight loss, and sold under the brand name of Menocil® (Karch, 2009; Rasmussen, 2008). It was rapidly withdrawn from the pharmaceuticals market after it became apparent that the compound could induce fatal pulmonary hypertension, sometimes after just 4 weeks of use, and there is currently no legitimate application for this medication (Karch, 2009; Rasmussen, 2008).

In the United States, it is occasionally sold to those who use illicit drugs under the guise of methamphetamine (Karch, 2009). It is easily synthesized, thus making it an attractive compound to manufacture in illicit drug labs, but it was classified as a Schedule I⁴⁴ compound in April 1989, and since then its use in the United States has been limited (Karch, 2009). Unfortunately, a medication used by veterinarians to deworm livestock, levamisole, is biotransformed into aminorex in humans. It is a frequent adulterant in compounds such as illicit cocaine or amphetamines. Drugs levamisole will expose the user to the same dangers inherent in aminorex misuse.

The effects of aminorex are not well documented, but do appear to be similar to those of the amphetamines or cocaine (Karch, 2009). Available evidence, based on research studies conducted before it was withdrawn from the market, suggest that aminorex is rapidly absorbed after an oral dose, with peak blood levels being seen approximately 2 hours after the drug is ingested. The reported half-life is approximately 7.7 hours (Karch, 2009), and it is excreted virtually unchanged by the

kidneys. Because of its legal status and potential for harm to the user, all clinical research into the effects of this compound was discontinued when it was withdrawn from the market. Its potential to cause other medical complications beyond pulmonary hypertension remains unknown at this time (Karch, 2009).

GAMMA HYDROXYBUTYRIC ACID (GHB)

This compound was first identified in 1960 when scientists were doing research on the neurotransmitter GABA. The chemical structure of GHB is very similar to that of GABA itself, which is not surprising in that it is metabolized from GABA, the main inhibitory neurotransmitter in the brain (Flower, Mendelson, & Galloway, 2009; Saunders, Connor, & Feeney, 2016). Similar to GHB, GLB (gamma butyrolactone) and 1,4-BD (1,4 butanediol) are precursors to GHB and are not typically misused (Saunders et al., 2016). Initially there was some interest in GHB as a presurgical agent since its effects were thought to be similar to those of GABA. However, the usefulness of this compound as a presurgical agent was very limited, because (a) many patients experienced vomiting and seizures when recovering from its effects, (b) it has a rather narrow therapeutic window,⁴⁵ and (c) when used in a surgical setting, other analgesics must still be administered to the patient (Tomb, 2008). These factors combined to make its use by physicians rather rare, although it is sold under the brand names Xyrem® and Alcover® in some countries for the treatment of *cataplexy*,⁴⁶ and at times for the treatment of AUDs (Saunders et al., 2016).

Small amounts of GHB are normally found in the human kidneys, heart, muscle tissues, and brain, and it is thought to function as a neurotransmitter in that organ (Drummer & Odell, 2001; McDowell, 2005). As a neurotransmitter, GHB helps to mediate the sleep cycle, body temperature, and cerebral glucose metabolism; it plays a role in the formation of memories, and was previously thought to stimulate the release of human growth hormone (Gahlinger, 2004; Karch, 2009; Saunders et al., 2016; Weaver & Schnoll, 2008). This latter effect was what made GHB use initially so attractive to muscle builders after the anabolic steroids were banned. Because of its widespread misuse, GHB was classified as a Schedule I compound⁴⁷ by the Drug Enforcement Administration in 2000, a move that might have contributed to the decrease of GHB use observed in

⁴³Technically, 2-amino-4-methyl-5-phenyl-2-oxazoline.

⁴⁴See Appendix 3.

⁴⁵The LD50 is only five times the therapeutic dose, thus making it easy for the individual to overdose on this compound. The therapeutic window is made even smaller if the person should be ingesting a CNS depressant such as alcohol simultaneously (Evans et al., 2005; McDowell, 2005).

⁴⁶See Glossary.

⁴⁷See Appendix 3.

the United States (van Noorden, van Dongen, Zitman, & Vergouwen, 2009). Instructions on how to make it are available over the internet, but there are different formulas used, and the potency and purity of the obtained product is often open to question. However, the majority of users report taking this compound for recreational purposes, given the sedative and intoxication effects (Karch, 2009; Saunders et al., 2016).

Clinically, it is well absorbed from the gastrointestinal tract following oral ingestion, but on occasion it is also injected intravenously by some individuals. When ingested orally, GHB's effects begin within 10–30 minutes. Peak blood plasma levels are seen in between 20 and 40 minutes following a single oral dose, and it has a half-life of approximately 20 minutes (Flowers et al., 2009; Karch, 2009). During the process of biotransformation, most of a single dose of GHB is excreted from the body as carbon dioxide, and only 2–5% is excreted from the body unchanged. GHB's short half-life, combined with its ability to induce amnesia and to escape detection by standard urine toxicology tests are all characteristics that originally made it attractive as a date rape drug. However, a urine test has been developed to detect GHB in the first 12 hours after it is administered, thus limiting its attractiveness as a date rape compound since law enforcement authorities now have the technique to identify its use (Gwinnell & Adamec, 2006; Karch, 2009).

Subjectively, the effects of GHB are similar to those of alcohol, producing effects such as drowsiness, a sense of euphoria, and disinhibition (Flowers et al., 2009; van Noorden et al., 2009). When used concurrently with alcohol at high doses, it is possible that high doses of GHB will inhibit the biotransformation of the alcohol. This increases the risk of a possible alcohol overdose, which may prove fatal (Karch, 2009). GHB may cause seizures if used simultaneously with methamphetamine (Smith, 2001). Patients with HIV infection and who are protease inhibitors should not ingest GHB, as the antiviral agents alter the user's ability to biotransform many compounds, including GHB (Drummer & Odell, 2001). Table 37-2 outlines some of GHB's effects on the user.

Additional side effects of GHB that have been reported include nausea, vomiting, tunnel vision, ataxia, confusion, agitation, dizziness, hypersalivation, hypotonia, and amnesia (Evans et al., 2005; Gahlinger, 2004). Conservative, supportive medical care is the best treatment for a GHB overdose, although intubation and restraints might be necessary in extreme cases (Miro, Nogue, Espinoza, To-Figueras, & Sanchez, 2002; Saunders et al., 2016).

Tolerance to GHB's effects develops rapidly. Individuals who use GHB long-term can become physically dependent

TABLE 37-2 GHB's Effects on the User

Dosage Level	Effect
0.1–1.5 mg/kg	Sleep state with enhanced delta and REM sleep
10 mg/kg	Euphoria, lowered inhibitions, amnesia (some reports of nausea, headache, itching, and vomiting reported at this dosage level)
20–30 mg/kg	In addition to above effects, light sleep and/or drowsiness
40–50 mg/kg	Deep sleep state
60–70 mg/kg	Deep coma, possible seizures
>70 mg/kg	Cardiopulmonary depression, seizures, respiratory depression, and possible death

SOURCE: Evans et al. (2005); Flowers et al. (2009); Koesters, Rogers, and Rajasingham (2002); Lehne (2013); Rosenthal and Solhkhah (2005).

on GHB, and there is a characteristic withdrawal syndrome that includes symptoms such as anxiety, tremor, insomnia, nausea, tachycardia, tremor, hypertension, and a delirium tremens–like syndrome in those who use GHB heavily and suddenly discontinue use (Freese et al., 2002; Klein & Kramer, 2004; Rosenthal & Solhkhah, 2005; Saunders et al., 2016; van Noorden et al., 2009). These symptoms usually begin within 12 hours of the person's last use of GHB, and can continue for up to 12–15 days. This withdrawal syndrome is potentially life-threatening (van Noorden et al., 2009). As the above information suggests, GHB is significantly more dangerous than was thought 20 or more years ago, and in spite of assurances from those who sell it, should not be misused.

METHOXETAMINE

Methoxetamine (3-MeO-2'-Oxo-PCE) is a chemical analog of ketamine that was originally developed as an alternative to ketamine itself. Its effects are assumed to be similar to those of ketamine and are thought to related to the antagonism of NMDA receptors (Wolff, 2016). When misused, its effects can last up to 7–8 hours (Troy, 2013).

Phenethylamines

There are more than 250 members of this family of compounds, including the natural compound mescaline, which is found in the peyote cactus of the American Southwest, the compound MDA, and the synthetic hallucinogen MDMA (Haroz & Greenberg, 2005; Strassman, 2005). Other members of this family of compounds include MDMA, DOET, DOB, 2C-I (and many others in this series), DOM, 5-APB, 6-APB, and many others (Brust, 2007b; Connor et al., 2016; Shulgin & Shulgin, 2007).

NEXUS

Nexus (2C-B; 4-bromo-2,5-dimethoxyphenethylamine)⁴⁸ is a well-known synthetic member of the phenylethylamines.⁴⁹ It has been a Schedule I compound since 1995. This compound is usually ingested orally, and a single dose of 10–20 mg will cause the user to experience intoxication, euphoria, and visual distortions or outright hallucinations for 6–8 hours. Doses above 50 mg result in extremely vivid, frightening hallucinations and morbid delusions (Karch, 2009). Side effects include nausea, abdominal cramps, pulmonary problems, and cough. In the brain, the compound shows an affinity for the serotonin 5-HT receptor subtype. Clinical research into the pharmacokinetics of this compound is very limited since it was never intended for human use (Dean, Stelpflug, Burnett, & Engebretsen, 2013). Detection of this compound through urine toxicology tests is difficult, since it does not react with many reagents used to identify various other drugs that are misused (Karch, 2009).

“BLUE MYSTIC”

Another member of the phenethylamine family of compounds is 2C-T-7,⁵⁰ known as “blue mystic” (Boyer, 2005). It is thought that this compound is about 12 times as potent a hallucinogen as mescaline. This compound is often used for its ability to induce visual hallucinations (Karch, 2009). Side effects can include nausea, cramps, seizures, and possible death from aspiration of material being regurgitated (Boyer, 2005). The difference between an effective dose and a toxic dose is only a matter of micrograms, which is to say that this compound has a very small “therapeutic” window, and little is known about the pharmacokinetics of this compound.

DOB

The compound DOB⁵¹ has effects similar to those of MDMA, but that last longer. Its use is largely confined to Australia, although on occasion it is found as a contaminant or adulterant to MDMA, or marketed as LSD (Karch, 2009). It is known that the effects begin 3–4 hours after the compound is ingested, and some of the symptoms might last for up to 24 hours (Karch, 2009; Shulgin & Shulkin, 2007). DOB use has been associated with blood vessel spasms and seizures, both of which have the potential to be fatal (Karch, 2009). It is significantly more toxic than LSD, but specific pharmacokinetic studies are lacking at this time.

PARAMETHOXYAMPHETAMINE (PMA)

This is a potent hallucinogen, and its hallucinogenic potential appears to be approximately the same as that of LSD (Karch, 2009). It is very toxic, and a number of deaths have been attributed to its use (Karch, 2009). Some of the adverse effects from the use of this compound include (Karch, 2009) tachycardia, hyperthermia, coma, seizures, arrhythmias, abnormal heart rhythm, and in isolated cases dangerously low blood sugar levels.

251-NOBME⁵²

This compound is often sold as a cheap alternative to LSD, or on occasion as LSD itself. Little is known about the pharmacokinetics or toxicology of this compound, although known side effects include coma, severe agitation, and delirium that potentially can last for days, aggression, tachycardia, respiratory acid, impaired kidney function, seizures, and death. Unlike LSD overdoses, where simple reassurance is often the best treatment and the effects usually wear off in 8–12 hours, a significant percentage of those who use 251-NOBME require treatment in the intensive care unit of a hospital for up to 5 days.

Tryptamines⁵³

There are at least 200 compounds in this family of chemical agents, all of which have a chemical structure similar to that of the neurotransmitter serotonin (Brown, 2007). Some of the compounds in this family of chemicals include the hallucinogen psilocybin, DMT, DET, psilocin, bufotenine, and 5-MeO-DALT. These compounds enjoyed various degrees of popularity in the 1960s and 1970s, but were classified as Schedule I⁵⁴ compounds by the Drug Enforcement Administration (Brust, 2007b; Haroz & Greenberg, 2005). Little is known about the pharmacokinetics of these compounds, although it is known that many of them are extensively biotransformed by the first-pass metabolism process, and must be snorted or smoked to be effective (Haroz & Greenberg, 2005; Mueller, 2005). All members of this family of compounds are able to induce the potentially lethal condition known as the **serotonin syndrome**.⁵⁵

One member of this family of compounds is known by a variety of names, including “foxy” or “foxy methoxy”⁵⁶ (Boyer, 2005; Meatherall & Sharma, 2005; Mueller, 2005). This compound appeared in the 1990s and was quickly classified as a Schedule I compound (Mueller, 2005). Unlike the other

⁴⁸Or 2,5-dimethoxyphenethylamine.

⁴⁹In some communities, it is sold under the name of Venus, bromo, erox, and XTC (Karch, 2009).

⁵⁰Or 2,5-dimethoxy-4-(n)propylthiophenethylamine.

⁵¹Or 4-bromo-2,5-dimethoxyamphetetramine.

⁵²Or 4-iodo-2,5-demethoxy-N-(methoxybenzyl)-phenylethylamine, or simply 251-NBOME.

⁵³Sometimes called the *indolealkylamines*.

⁵⁴See Appendix 3.

⁵⁵See Glossary.

⁵⁶Or 5-methoxy-N,N-diisopropyltryptamine.

tryptamines, foxy is not significantly affected by the first-pass metabolism effect, and can be ingested orally. Although this compound has a different chemical structure than MDMA, the effects are very similar for the individual, and it has the same potential for neurological damage as does ecstasy. Little is known about the pharmacokinetics of this compound. It is known that when ingested orally, the effects begin in about 20–30 minutes (Mueller, 2005). The main effects are thought to be the result of this compound's ability to act as a serotonin 5-HT_{2a} receptor agonist. It can cause sexual stimulation and mild hallucinations, which are the desired effects. Side effects include (but are not limited to) (Meatherall & Sharma, 2005; Mueller, 2005) anxiety, restlessness, insomnia, a fear of imminent death, and possible seizures. There is evidence suggesting a synergistic effect between foxy and compounds such as PCP, ketamine, and marijuana, but little is known about the pharmacokinetics of this compound, either in isolation or in combination with these substances.

PSILOCYBIN

Psilocybin is a naturally occurring tryptamine compound found in the mushroom *Psilocybe mexicana*, which is found in the northern part of Mexico and the Southwestern United States. The Aztecs called psilocybin the “flesh of the gods,” suggesting that they were quite familiar with this compound and its ability to induce a mystical state of mind in the user (Griffiths, Richards, McCann, & Jesse, 2006). Research into the pharmacokinetics of psilocybin ended in the 1960s for the most part, although there has been a recent resurgence in investigations to consider whether it has any treatment benefits. It is known that high doses can induce seizures and confusional states, but fatalities that occur after the ingestion of psilocybin are most often the result of accidents or suicide rather than the direct effects of the compound (Filley, 2004).

Designer Narcotics

Fentanyl

Fentanyl is a synthetic opioid that is widely used in various medical procedures. The basic fentanyl molecule is one that can be manufactured from a few ordinary industrial chemicals, although the process is rather difficult and lends itself to errors in the production process (Karch, 2009). The high potency of fentanyl can result in unintentional drug overdoses, some of which might be rapidly fatal, as has recently been seen in the United States (Peterson et al., 2016). For example, when smoked (a popular method of fentanyl misuse), it is possible for one inhalation to prove fatal to the individual because of the potency of the compound (“Take time to smell the fentanyl,” 2004).

By making just a minor change in the basic fentanyl molecule, it is possible to produce fentanyl analogs with various psychoactive effects. One analog has been found to extend fentanyl's effects from the normal 30–90 minutes to 4–5 hours. Another fentanyl analog extends the effects to 4–5 days. The compound 3-methyl fentanyl (or TMF) is thought to be about 6,000 times as potent as morphine, a characteristic that makes it a popular drug for snorting (Ruzycki, Yarema, Dunham, Sadrzadeh, & Tremblay, 2016). While these fentanyl analogs can be produced using easily available industrial chemicals, a simple mistake in the production process can produce compounds that are toxic and possibly fatal to the user. Another analog of fentanyl is acetyl fentanyl, a compound that is reputed to be five times as potent as heroin (Ogilvie et al., 2013). This compound is a Schedule I compound. The DEA has also recently placed the analog furanyl fentanyl on Schedule I due to the significant number of deaths related to this compound (Drug Enforcement Administration, 2016d). Of even more concern is the analog carfentanil, which is said to be 10,000 more potent than morphine, and 100 times the potency of fentanyl; it is a Schedule II drug (Drug Enforcement Administration, 2016c, 2016d). “Pink,” U-47700, is another synthetic opioid that only recently surfaced as a designer drug, and was quickly listed as Schedule I in 2016 following almost 50 deaths in a number of states (Grover, 2016).

Dextromethorphan (DXM)

This is a synthetic compound, which is a chemical cousin to codeine. There are many different street names, including CCC, triple C, skittles, robo, and poor man's PCP (Drug Enforcement Administration, 2014). It is not a controlled compound as of this time (Drug Enforcement Administration, 2014; Karch, 2009). Dextromethorphan was originally marketed in the 1960s as an antitussive compound for the treatment of mild to moderate-intensity coughs, either alone or in combination with therapeutic doses of such compounds as antihistamines (Haroz & Greenberg, 2005; Stanciu & Penders, 2015). Normal adult doses are about 30 mg every 4–6 hours. It is a relatively effective cough suppressant, and more than 140 over-the-counter compounds sold in the United States alone contain dextromethorphan either as the primary or one of the primary ingredients (Bobo, Miller, & Martin, 2005).

Dextromethorphan tends to concentrate in the brain, and the concentration of DXM in the brain is significantly higher than that found in the blood plasma (Karch, 2009). This is the site of its cough suppressant effects. DXM is biotransformed in the liver and is a prodrug with the active metabolite *dextrorphan* inducing its cough suppressant effects (Karch, 2009). This compound is extensively deactivated

by the first-pass metabolism effect (Karch, 2009). However, about 10% of the general population lacks the ability to produce an enzyme⁵⁷ necessary to biotransform dextromethorphan and are classified as slow metabolizers of this compound (Karch, 2009, p. 605). Whereas the effects of a typical dose of DXM last 4–6 hours in the average person, a single therapeutic dose will last 17–22 hours in a person deficient in this enzyme. The implications of this are especially important when one considers the dosage levels utilized by those who use DXM (discussed below). On rare occasions, DXM can also induce the serotonin syndrome.

DXM is frequently misused by adolescents, a process called “robotripping” (Stanciu & Penders, 2015; Storck, Black, & Liddell, 2016). A powdered form of DXM is available over the internet, and there are websites that will give step-by-step instructions on how to use DXM and what effects to look for at different dosage levels (“Escalating DXM abuse among teenagers,” 2007). The peak age of DXM use is about 15–16 years of age (Bryner et al., 2006). However, in contrast to the therapeutic dosage level of 30 mg every 3–4 hours, those who misuse DXM routinely ingest doses of between 150 and 2,000 mg at one time (Brust, 2004).

In the brain, DXM functions as a **NMDA**⁵⁸ channel blocker and a serotonin reuptake blocker (Brust, 2004). At dosage levels of between 300 and 1,000 mg/kg of body weight, the effects of DXM are similar to those of PCP or its chemical cousin ketamine, inducing a dissociative experience (Bobo et al., 2005; Stanciu & Penders, 2015). The effects begin within 15–30 minutes, and last for 2–6 hours (Haroz & Greenberg, 2005). Adverse consequences of DXM when used include disorientation, panic attacks, paranoia, slurred speech, hostility, ataxia, tremor, nausea, vomiting, and nystagmus (Bobo et al., 2005; Stanciu & Penders, 2015). A DXM overdose⁵⁹ might produce such symptoms as: lethargy, slurred speech, hyperexcitability, ataxia, tremor, rigidity, tachycardia, hypertension, nystagmus, respiratory depression, acute psychosis, coma, and possible death from cardiovascular collapse. As with any substance, all cases of possible dextromethorphan overdose should be assessed by a physician immediately. Another issue to consider when reviewing the toxic effects of DXM is the possibility that the agent in which it is mixed (cough syrup) might contain other compounds (acetaminophen, for example) that are also toxic if used to excess.

⁵⁷CYP2D6, which is part of the metabolic P-450 pathway of the liver.

⁵⁸See Glossary.

⁵⁹If the DXM was in a preparation that also included acetaminophen, which is common for many over-the-counter cough and cold medications, the misuser will be at risk for unknowingly ingesting an acetaminophen overdose (discussed in Chapter 18).

Hydromorphone⁶⁰

This is a semisynthetic narcotic used for moderate and severe pain. Research into the pharmacology of hydromorphone is limited, although it is known to bind at the mu opioid receptor site and thus potentially can suppress the respiratory reflex, and in extreme cases can cause death by respiratory depression. Its misuse potential is approximately the same as that of oxycodone, and if extended-release tablets are crushed or chewed, all of the medication is released into the body at once, possibly inducing a fatal overdose. Should the individual also be using another central nervous system depressant, the risk of overdose is markedly increased. It is currently a DEA Schedule II substance.

Desomorphine

This synthetic morphine analog has been in existence since 1932, but did not appear as a drug of misuse until 2002 (Drug Enforcement Administration, 2013b; Rech et al., 2015). It is often referred to as “krokodil,” or “crocodile,” referring to the skin of those who have misused the substance on an ongoing basis (Drug Enforcement Administration, 2013b). This substance is stronger than heroin, and is considered to be 10 times as potent as morphine (Rech et al., 2015). It is a Schedule I substance at this time.

Kratom

Kratom is an herbal product derived from the leaves of the *Mitragyna speciosa* plant, which grows in Southeast Asia (Troy, 2013). It is often referred to by the street names biak-biak, ketum, kahum, or thom (Rech et al., 2015). Although the leaves of the plant contain a number of alkaloids, the pharmacokinetics of the most potent of these alkaloids, mitragynine and 7-hydroxymitragynine, have not been explored. Both of these compounds appear to function as mu opioid receptor agonists. Mitragynine is thought to be 13 times as potent as morphine, while 7-hydroxymitragynine is thought to only be four times as potent as morphine. The leaves may be powdered and smoked, mixed with regular tobacco, or brewed as a tea or other beverage (Troy, 2013). The effects appear to be dose-dependent, with lower dosage levels having a mild stimulant effect, while higher doses produce a more traditional opioid-like effect (Troy, 2013). The DEA indicated its intent in 2016 to add kratom to the Schedule I list (Drug Enforcement Administration, 2016b, 2016d), but they have not yet done so.

⁶⁰Although hydromorphone is a legitimate pharmaceutical, it is also frequently diverted to illicit markets, or misused by the individual taking the medication. For these reasons it is included in this section.

Salvia (Salvinorin A and *Salvia Divinorum*)

This hallucinogen is also plant-based, and is often called Sally-D, magic mint, or diviner's sage, among other names (Rech et al., 2015). It is not currently a DEA scheduled drug, but many states have enacted controls for this substance (Drug Enforcement Administration, 2013a). Research to date does indicate that there may be a potential for this substance to expose or aggravate psychiatric disorders and psychosis (Rech et al., 2015).

Atypical Compounds of Misuse

Atypical Antipsychotic Compounds

Although rarely considered potential agents of misuse, there is evidence based on patient case studies suggesting that some individuals are misusing a class of medications known as atypical antipsychotic medications as drugs of misuse. Some patients have been known to “cheek”⁶¹ prescribed antipsychotic medications to save the pills or capsules. When they have enough, they take what is technically an overdose, not as part of a suicide attempt but for the ability of these medications to induce perceptual distortions. A second group of individuals will use these medications to enhance the effects of more traditional drugs of misuse.

Fry

There have been isolated reports of this compound in the United States. Fry is essentially marijuana soaked in formaldehyde, and then laced with PCP (Klein & Kramer, 2004). While euphoria is the desired effect of this mixture, it can produce a toxic psychosis, hallucinations, delusional thinking, panic, paranoia, reduced attention span, loss of consciousness, and brain and lung damage (Klein & Kramer, 2004).

Benzypiperazine (BZP)

BZP is misused for its euphoric and amphetamine-like effects. Available evidence suggests that it was originally considered as a compound to treat intestinal parasites in cattle, but its potent side effects made researchers lose interest in the compound. It is often used for its MDMA-like effects, affecting both the serotonergic and dopaminergic receptor sites. Subjective effects are identified in Table 37-3.

TABLE 37-3 Some Side Effects of BZP Misuse

Milder	Severe
Anxiety	Hyperthermia
Agitation	Psychosis
CNS stimulation	Renal toxicity
Confusion	Respiratory failure
Dilated pupils	Rhabdomyolysis
Dry mouth	Seizures
Headache	Serotonin syndrome
Hyperventilation	
Hypothermia	
Insomnia	
Nausea/vomiting	
Tachycardia	
Urinary retention	

Other atypical drugs of misuse include any of a wide range of antihistamines, quetiapine, olanzapine, and any of the tricyclic antidepressants, which are occasionally used for their sedating effects at higher than normal doses (Reeves, Ladner, Perry, Burke, & Laizer, 2015). The antiseizure medication gabapentin, pseudoephedrine, and the selective serotonin reuptake inhibitor antidepressants fluoxetine and venlafaxine are occasional used for their central nervous system stimulant effects when taken at above normal doses. Dextromethorphan⁶² and the anticholinergic medications⁶³ are used for their ability to induce a dissociative state, while quetiapine is often used to augment the effects of opiates, and those compounds with a sedating effect might be used to control the stimulant effect of cocaine when it becomes aversive to the individual (Reeves et al., 2015). There is only limited information on the effects of these compounds when they are misused at higher than normal levels.

Medication Diversion

Individuals who misuse medications may know the physician's schedule, and know exactly when to come to the office or the emergency room with exaggerated signs of physical distress. They do so in the hope of obtaining a prescription from the overworked physician, who is looking forward to the end of the shift or day. Such medical emergencies are often seen on Fridays at 4 p.m., for example, and the narcotics addict hopes that the physician will just write out a prescription rather than

⁶¹Hide a tablet or capsule under the tongue, or between the teeth and cheek of the mouth.

⁶²Discussed earlier in this chapter.

⁶³Used to treat the side effects of the tricyclic antidepressants.

spend time arguing with the person. Claims of physician abandonment are often intermixed with threats, and exaggerated complaints of physical illness are used to obtain the desired prescriptions. These behaviors, plus reports that the person is “allergic” to less powerful narcotic analgesics such as tramadol, or that these compounds do not work for the person, should alert the physician to the possibility of drug-seeking behaviors. Still, because it is the end of the shift, there is a small mountain of paperwork waiting to be filled out, and the physician wants to go home, it is not uncommon for the physician to write out a prescription just to get the person to leave.

The diversion of prescribed narcotic analgesics has become a major problem in recent years. The individual’s motivation for abusing prescribed narcotic analgesics, especially methadone, ranges from a desire to obtain narcotic-induced euphoria to attempts to taper themselves from narcotic analgesics using illicit compounds (Davis & Johnson, 2008). Some individuals use illicit opioids to self-medicate pain, according to the authors. The authors found that 72% of the subjects in their study used methadone, and 65% sold it. Indeed, the authors found that methadone misuse was more common than that of OxyContin, Vicodin, or Percocet. Recently, the author introduced a reformulated form of OxyContin that hopefully will make its misuse more difficult.

An Emerging Danger

At this time, there has been no evidence of illicit drugs being produced by genetically engineered⁶⁴ microorganisms; however, scientists anticipate that such compounds will begin to appear in a decade or less (Le Page, 2015). This process could allow yeast cells to be genetically modified to produce large amounts of both existing drugs of misuse and novel chemicals that might prove superior to existing drugs of misuse (Le Page, 2015). Unfortunately, this process will also allow illicit chemists to use the same techniques to develop strains of a microorganism such as yeast to produce compounds that will prove to be much more potent and more addictive than the chemicals currently being misused, or offer novel pharmacokinetic properties that will make their misuse more attractive to the individual (Le Page, 2015). Equally disquieting is the fact that this process will allow for these compounds to be produced locally, complicating the efforts of law enforcement agency interdiction of these compounds. Other implications of this impending flood of illicit chemicals produced by genetically altered microorganisms are unknown at this time.

⁶⁴The process of genetic engineering involves taking selected genes from one microorganism and inserting them into another to alter its function.

Chapter Summary

The relationship between criminal activity and substance use disorders is quite complex, and worthy of a book in its own right. The debate over whether those people most prone to criminal activity are drawn to the SUDs as well, or if criminal activity is a consequence of the lifestyle forced on those who wish to engage in substance misuse, continues to rage. Currently, it appears that both are applicable, depending on the individual and his or her path toward addiction to a chemical.

At least some of the harm associated with the SUDs is a direct result of society’s efforts at supply reduction through the “war” on drugs. By making chemical misuse illegal, society has both generated a new class of criminals (the misusers), and helped the growth of a class of criminals associated with the sale and distribution of drugs. Because it is a closed, illegal market, upper- and middle-level drug dealers often add various adulterants to the product that ultimately is sold to the individual using illicit drugs. These adulterants cause or contribute to various health consequences for the individual, who then seeks medical assistance. This, in turn, places an additional burden on the health care system. There have been significant unanticipated consequences from making drugs of misuse illegal.

Further, to avoid criminal prosecution, those involved in the drug distribution industry have been searching for new “designer” drugs, which have yet to be banned. When these compounds are identified by law enforcement officials and then outlawed, the search for other designer compounds that have not been banned begins anew. This search is spurred on by the criminal sanctions in place against the distribution and sale of illegal compounds. However, enforcement of these sanctions has resulted in further demands on the overburdened court system, which will be discussed in the next chapter. Some of the more commonly encountered designer drugs, and their effects, were reviewed.

The diversion of prescribed narcotic analgesics has become a major problem in recent years. The individual’s motivation for abusing prescribed narcotic analgesics, especially methadone, ranges from a desire to obtain narcotic-induced euphoria to attempts to taper themselves from narcotic analgesics using illicit compounds (Davis & Johnson, 2008). Other persons are using the opioids to self-medicate pain, according to the authors. Seventy-two percent of the subjects in their study used methadone, and 65% sold it. Indeed, the authors found that methadone misuse was more common than that of OxyContin, Vicodin, or Percocet. The findings of this study underscore the problem of the diversion of prescribed narcotic analgesics.



CHAPTER 38

The Debate over Legalization¹

LEARNING OBJECTIVES

After studying this chapter, students should be able to:

- 38.1** Understand both sides of the debate related to legalization
- 38.2** Review the history of the “war on drugs”
- 38.3** Consider the impact of the “war on drugs”
- 38.4** Review the debate over medical marijuana
- 38.5** Understand the status of recreational marijuana

When the United States is not invading some sovereign nation—or setting it on fire from the air, which is more fun for our simple-minded pilots—we’re usually busy “declaring war” on something here at home.

Anything we don’t like about ourselves, we declare war on it. We don’t do anything about it, we just declare war. “Declaring war” is our only public metaphor for problem solving. We have a war on crime, a war on poverty, a war on litter, a war on cancer, a war on violence, and [President] Ronald Reagan’s ultimate joke, the war on drugs. More accurately, the war on the Constitution.

Carlin (2001, p. 109)

Introduction

The late comedian George Carlin was, in the opinion of many, at his best when he was poking fun at social and political trends. However, in a very real sense the quote at the start of this chapter is more than just a joke. The substance use disorders are the only medical (or psychiatric) condition in which the manifestations of the illness (in this case alcohol misuse or illicit drug use) is addressed through the legal system (Heyman, 2009). A person with diabetes, a seizure disorder, or cancer does not need to fear arrest for experiencing a seizure, being diabetic, or having cancer. However, the person with a substance use disorder with heroin use, for example, is in danger of facing legal charges for engaging in the very behaviors that the medical field defines as the disease!

¹It is not the purpose of this chapter to advocate the legalization of compounds currently deemed illegal. Rather, it is the purpose of this chapter to stir debate as to the question of legalization.

A rational perspective on the problem of illicit drugs is “generally lacking” when the problem of illicit drugs is considered (“Drugs drive politicians out of their minds,” 2009, p. 5), although there has certainly been a shift over the past decades regarding marijuana in particular (Gruber & Sagar, 2017). In this chapter, we will briefly explore the controversy surrounding the question of legalization of at least some of the current drugs.

Statement of the Problem

The battle lines have been drawn: There are those in the United States who believe that “[w]hat you do with your consciousness is your own business” (Amanda Feilding, an early researcher specializing in the study of psychoactive drugs, quoted in Lawton, 2013, p. 37). In contrast to this rather tolerant view are those who have responded almost with a military-like program of extermination: Those who misuse substances classified as illegal are subject to legal sanctions, the exact nature of which is dependent upon where the alleged crime took place.

It is widely acknowledged that addressing the substance use disorders through legal sanctions is not effective: The link between criminal penalties and the substance use disorders is weak, at best (Taverne, 2010). In the United States, there is now movement toward court systems that problem-solve, and that work toward improving substance use disorder treatment for those who need such help in the criminal justice system (Pollack, 2016). However, there is still often a reactionary response to problems that arise related to drugs, as many social policy decisions are made on the basis of media reports that are biased or misleading (Szalavitz, 2014). Whereas social scientists call for a more rational policy addressing the substance use disorders, some governments choose to listen to the loud, moralistic, special interest groups that warn that to change existing policies on illicit drugs is to be “soft on crime” (“Drugs drive politicians out of their minds,” 2009; Taverne, 2010).

When a government bans a certain behavior or substance, it is attempting in effect to protect the citizens from the consequences of their own choices. In the case of the drugs of misuse, the rewards for engaging in this behavior are rapid, and the “law can rarely reform a people who have already succumbed to the allures of immediate gratification”² (Woods, 2005, p. 212). That reality is ignored as law enforcement officials and politicians have called for

stronger and more draconian measures to “win the war on drugs.” The logic behind this approach has repeatedly been criticized, with little movement by leaders until recent years. Further, as will be discussed later in this chapter, the problem of illicit drug use has been used as an excuse to negate many of the provisions of the U.S. Constitution and the Bill of Rights. Many nonviolent offenders have been sentenced to jail or prison on the pretense that this action will protect the public from those who use illicit drugs.³ To make room in the prison for these nonviolent individuals, those with violent criminal histories have been, out of necessity, released from prison before completion of their sentences.

The “success” of these tactics may be seen in the fact that the United States is the leading consumer of cocaine, Colombian and Mexican heroin, as well as Mexican marijuana, and is also considered a money-laundering center (Central Intelligence Agency, n.d.). Globally, the illicit drug market has been estimated to be a \$400 billion dollar-a-year industry (United Nations, 2011), although there is certainly controversy about this figure as it is quite a challenge to estimate an industry that operates overall on a cash basis. If the United States consumes two-thirds of the world’s illicit drugs (Dobbs, 2007), then our share of this illicit drug trade is \$266 billion each year. The United States is also spending at billions each year to fight the “war on drugs,” with more than a trillion dollars spent since 1971. In the next section we will examine the impact that this expenditure has had on the illicit drug trade.

The “War” on Drugs: An Ongoing National Disaster

Future historians will view the “war” on drugs with disbelief. This war has raged for the better part of a century. It continues not because of the destructive potential of the drugs, but because of the irrational beliefs of those in command. An example of this was the social movement to legalize marijuana in the United States in the early 1970s. Then President Richard M. Nixon refused to consider this possibility because of a personal belief that (a) people who consume alcohol do not use it for its intoxicating effects but for fun, while (b) people who used marijuana were mainly those who were protesting against the then-current Vietnam War and whose substance use was part of the reason why they were protesting

²The quote referenced the immorality of Roman society under Caesar Augustus; however, it appears to be equally applicable in this setting.

³Heyman (2009) argued that the majority of those who are incarcerated are in prison for the crime of *drug sales* and not possession of a controlled substance. While it is tempting to argue that this will reduce drug availability, evidence suggests that it is at most a temporary solution, since other drug dealers quickly move in to fill the void.

(Zeese, 2002).⁴ There were also subtle racial undertones to the antidrug efforts of the Nixon administration, which were only discovered in the early years of the 21st century (Zeese, 2002). For example, possession of powdered cocaine (most prevalent in middle-class America) resulted in a much more lenient sentence than possession of an equal amount of “crack” cocaine (most prevalent in the inner cities).

The War on Drugs: The Fantasy

The war on drugs is based on four legs: (a) elimination of illicit compounds through destruction of raw materials, (b) the interdiction of drugs being shipped to this country, (c) legal sanctions against those who engage in the use of the substances deemed illegal by the government, and (d) treatment of individuals addicted to these compounds. We will examine each of these legs supporting the “war on drugs” in turn.

1. Elimination of Raw Materials

As a tactic, the elimination of the raw materials used to produce the illicit drugs makes sense. If you eliminate the raw materials, then the compound cannot be produced, and the problem is solved. The reality is far different. For example, a program started in the 1990s to eradicate cocaine cultivation in Colombia by spraying the fields where the coca plant is cultivated with an herbicide proved to be a costly failure (Mejía, 2015). The farmers managed to adjust to the potential of their crops being sprayed by a number of different methods. In some cases, they just moved over to the next valley, and started to cultivate the coca plant there. Over time, additional methods allowed for continued growth: Use of molasses on the plants prevented the herbicide from working; cutting the plant shortly after being sprayed allowed for regrowth of the lost product within months; and they prepared additional seedlings ready to plant (Mejía, 2015).

Many compounds are manufactured from precursor chemicals that are often legally obtained. An example of the failure of precursor elimination may be seen in the ongoing battle over ephedrine and similar products. Ephedrine can be used in the production of methamphetamine and was briefly classified as a controlled substance in the United States. As a result of this decision, producers of illicit methamphetamine either (a) moved the production center to other countries where ephedrine is easily available, or (b) changed the process of producing methamphetamine

to use pseudoephedrine, an over-the-counter cold remedy. This then resulted in the reaction of the government to mandate selling products containing pseudoephedrine only from behind the counter, and limiting the amount someone can purchase at one time. Thus, since that time there have been methods devised to make small batches of methamphetamine. These (and a multitude of other) examples all suggest that the elimination of those products used in the production of illicit drugs has failed. However, this effort is necessary,

because some of the plants that grow in the southern hemisphere are just plain evil. We know that because they're not stamped with labels like Bristol-Meyers, Squibb, Eli Lilly or Pfizer. And it's vital that we understand that these southern hemisphere plants and their cultivators are to blame because the alternative is to believe that our national appetite for drugs is *our own problem*. And that's plain crazy talk.

Maher (2002, p. 49, italics added)

As should be readily apparent by now, efforts at elimination of the raw materials used to produce the world's illicit drugs has been a failure, and as the quote above indicates, may be avoiding the true issue.

2. Interdiction

THE LESSONS OF HISTORY: PROHIBITION

The pages of history provide stunning evidence that the interdiction of illicit compounds is doomed to failure. The clearest example of this failure was the “Great Experiment” of Prohibition, or simply Prohibition,⁵ which began in 1920 and ended in 1933.⁶ This social experiment was based on the theory that many of society's ills were caused by alcohol (“Demon Rum”), the result being that the nonmedical use of alcohol was outlawed. Even when prescribed by physicians, patients might receive only one pint of liquor every 10 days (Pain, 2008). Because of this law, more than one physician concluded that his medical school education was negated by “a few farmers, lawyers, politicians and the like . . . who have the audacity to say to the medical profession of this country

⁵ Technically the bill was called the Volstead Act of 1919.

⁶ To his credit, Prohibition was passed over the veto of then-President Woodrow Wilson. Many members of Congress, and Wilson's successor President Warren G. Harding, were what Okrent (2010) called “dry-wets.” In public they espoused the benefits and goals of Prohibition, while openly flouting the law by maintaining bars well stocked from the best liquor captured by federal agents who interdicted alcohol shipments into the United States. However, Congress often does exempt itself from laws passed to benefit the lowly citizens who voted for them.

⁴ Would it come as a surprise to learn that President Richard M. Nixon was known to drink liquor on many occasions? Go figure.

that they can't prescribe this or that" (unknown physician, quoted in Pain, 2008, p. 45).⁷

Although Prohibition began in 1920, the per capita consumption of beer in the United States had reached its low point between 1911 and 1914 (Schweikart, 2008). The number of deaths from cirrhosis of the liver reached its lowest levels in 1921, just a year after the start of Prohibition.⁸ Further, by the end of Prohibition, medical journal articles on alcohol had all but disappeared (Schweikart, 2008). One could argue that Congress willingly "closed the bar door after the horse was out," since Prohibition was passed after the problem had begun to resolve itself. Admittedly, the level of alcohol consumption continued to fall during the Prohibition years, but only by approximately 30% (Okrent, 2010; Schweikart, 2008).

So great was the demand for alcohol that, at its height during Prohibition, the distribution of illegal alcohol made up 5% of the nation's gross national product (Schlosser, 2003). enforcement of the Volstead Act of 1919⁹ began to waver in the face of a tidal wave of illegal alcohol, so Congress passed what is known as the Jones Law to stiffen the penalties for violation of Prohibition laws. In many cases, what were formerly misdemeanors were transformed into felonies under the Jones Law. An unintended consequence of this step, however, was that the small-time producer or transporter of alcohol was replaced by organized crime syndicates. Nor was this the only unanticipated consequence of Prohibition: Following the start of Prohibition the homicide rate in the United States increased fourfold, while other forms of crime increased by 24% (McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds, 2009). Arguably, Prohibition did little more than contribute to a staggering increase in corruption among elected officials and law enforcement officers, a decline in civil rights, and profits for what might loosely be called "organized crime" (Lessig, 2009). It also eliminated a source of tax revenue for the government.

Before the start of Prohibition, the activities of organized crime had mainly been limited to prostitution and illegal gambling. The emerging organized crime organizations, sensing huge profits in providing alcohol to those who wished to drink in spite of Prohibition, quickly took control of the emerging illicit distribution system (Gray, 1998). Organized crime was armed with bribery money and high-powered

attorneys to fight criminal charges should they be caught breaking the law (Okrent, 2010). These syndicates also rapidly started to fight among themselves to gain control of territories in which to distribute illegal alcohol. On occasion, these territorial "negotiations" were aided by the judicious use of explosives or automatic weapons fire from vehicles driving past a competitor's place of business.¹⁰

Another totally unanticipated consequence of Prohibition was that it forced those people who wanted to consume alcohol to switch from beer to hard liquor (Gray, 1998; McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds et al., 2009). This is consistent with the theory that successful interdiction efforts might cause dealers to *increase* the potency of their product to encourage customer loyalty because of the difficulty of finding new customers during a time of increased police surveillance (Giles, 2009). With alcohol, liquor presented the appeal of having less bulk, a higher alcohol content, and it did not spoil as rapidly as did beer. Before the start of Prohibition, the typical drinker would sip their drinks over an extended period, without evidence of widespread intoxication (Barr, 1999; Gray, 1998). With the start of Prohibition, drinkers shifted to a pattern of binge drinking, with the goal of rapidly achieving a state of intoxication (Barr, 1999; Gray, 1998). At the same time, individuals who did drink switched from beer to liquor, which allowed them to achieve the highest level of intoxication in the least amount of time (Gray, 1998). When Prohibition ended, drinkers retained this pattern of alcohol consumption. In this manner, the Great Experiment helped to shape the drinking habits of people for generations to come.

RECENT DECADES

Starting in the 1970s, a phenomenon similar to that seen in Prohibition evolved, although the parallels with the Prohibition era were not recognized until much later. History shows that the interdiction efforts of law enforcement authorities encouraged drug smugglers to switch from bulky, low-profit marijuana to cocaine. Pound for pound, cocaine is less bulky, less smelly, more compact, and more lucrative to smuggle into the United States. Further, the interdiction efforts against cocaine dealers appear to have contributed to the development of drug gangs and a wave of violence that swept across the country in the 1980s and 1990s (Brust, 2004). By arresting the older, established drug dealers, the way was opened for inner-city, violence-prone, younger drug dealers to move into the business of selling cocaine, and to fighting over "turf" (Brust, 2004).

Another example of the "Law of Unanticipated Consequences" might be seen in the efforts of law enforcement officials to interdict methamphetamine production in the

⁷ This is a charge that has been repeated when physicians encountered the federal ban against prescription marijuana.

⁸ As was discussed in Chapter 5, it takes a number of years of chronic alcohol use for liver cirrhosis to develop. The fact that cases of cirrhosis reached their low point in 1921 is indirect evidence that alcohol use had been falling before the start of Prohibition in 1920.

⁹ For better or worse, Andrew Volstead was the congressman who was credited with writing the Prohibition laws.

¹⁰ Which sounds vaguely like the current situation between gangs selling drugs on street corners, or in crack houses, does it not?

United States. In the 1990s, much of the methamphetamine was produced in small “mom-and-pop” laboratories that produced small amounts of methamphetamine for local consumption. By making these facilities a focus for law enforcement, the manufacture of methamphetamine was switched to “superlabs” outside the United States that are capable of producing large amounts of relatively pure methamphetamine to be smuggled into this country (McPherson, Afsarifar, Hall, Yudko, & Rodriguez, 2009; Smith, 2006).

Only a small percentage of the drugs that are produced and sent to be smuggled into this country are interdicted, and at best this only results in short-term, local reductions in drug availability. Given the level of profits involved, if one drug supplier is arrested, another will step into the void to sell drugs to those who desire them. The interdiction policies ignore the facts that (a) the more “effective” police activity is, the more drug prices rise, (b) increasing the profits of smuggling and distribution of the product to meet demand, and further, (c) the more likely drug purity and concentration will also increase (d) to make importation more cost-effective and detection more difficult (Kleiman, 2011). This was a lesson that law enforcement officials and those who make policy could have learned from Prohibition had they but stopped to reflect on history: Interdiction just does not work (Reuter, 2009). Frances (2013) rated the interdiction campaign as “no more than a phony Whac-A-Mole charade” (p. 210), which has made many drug suppliers very wealthy.

In return for taking the risk of criminal prosecution, high-level suppliers arrange for drugs to be manufactured or smuggled into this country (usually by surrogates), where they are delivered to major cities and then funneled to outlying regions by middle-level distributors (Furst, Herrmann, Leung, Galea, & Hunt, 2004). The distributor at each level charges a high price for this service, which ultimately is passed on to the consumer. The product mark-up is rather high, and is justified by the dealer’s risk of arrest and prosecution. If one distributor is arrested, another person interested in such profits will simply step into the void.

3. Criminalization

There is little evidence that criminalization reduces illicit substance use (Taverne, 2010). In spite of this fact, criminalization remains a cornerstone of the war on drugs. The fact that it turns otherwise law-abiding people into criminals is quietly ignored. However, since the misuse of illicit drugs is by definition illegal, those who misuse an illicit drug are classified as criminals for engaging in the very behavior used to define addiction as a disease. A person does not need to engage in the sale, manufacture, or distribution of illicit drugs. They are criminals just because they use a compound defined as illicit, and at best are pushed to the fringes of society.

Because drugs are illegal and not freely available, individuals with an SUD are then forced to use their drug(s) of choice under conditions that contribute to health care problems. Although the drugs can cause terrible damage to the user’s body, the conditions under which the individual uses these illicit compounds cause additional health care problems, becoming another indirect cost of the war on drugs. Further, since by definition the illicit drugs are illegal, the individual may resort to criminal activity to support her or his SUD. Paradoxically, these consequences of the criminalization of certain compounds are then used to justify keeping them illegal.

The methods used by law enforcement authorities involved in the war on drugs are hardly respectful of those who are addicted to these compounds. It has been suggested that the drug enforcement agencies in the United States, especially the Drug Enforcement Administration, have become “as cruel as the rapacious drug dealers who just try to make money” (Doblin, quoted in Froom, 2008, p. 43). Most certainly, there is a definite lack of respect for those who, by definition, suffer from the medical disease known as addiction. In other words, to “win” the war on drugs, we have become just as violent and indifferent as the “enemy.”

MANDATORY SENTENCING

The “link between criminal penalties and drug use is weak” (Taverne, 2010, p. 26). On the basis of this dubious connection, though, Congress authorized the execution of heroin dealers to stem the tide of narcotics misuse in the United States following World War II, and a few heroin dealers were executed (Walton, 2002). In spite of this drastic sanction, the number of individuals using narcotics in the United States continued to increase (Walton, 2002). In the 1950s, Congress passed a new series of mandatory sentencing laws that dictated minimum sentences to be imposed on narcotics dealers. These laws met with almost universal acceptance, and were loosely called the Boggs Act.¹¹ These laws were passed on the dubious assumption that it is possible to punish undesirable behaviors out of existence (Husak, 2004; Lundeen, 2002).

One dissenting voice to the Boggs Act was that of James V. Bennett, the director of the U.S. Bureau of Prisons. He expressed strong reservations about the possible effectiveness of the Boggs Act. Although he had not broken any laws in doing so, he was subsequently followed by agents of the Federal Bureau of Narcotics, who submitted regular reports to their superiors on the content of speeches that he made. In spite of the enthusiasm with which the Boggs Act was received and the reports filed by Federal Bureau of Narcotics agents on the content of Mr. Bennett’s views, it had become clear that

¹¹ Named after the congressmen who first proposed the legislation. This proposal became law in 1952.

Mr. Bennett was right: Mandatory minimum sentencing did little if anything to reduce the scope of narcotics use in the United States. Congress then replaced the Boggs Act with a set of sentencing guidelines that allowed the presiding judge to assign appropriate sentences based on the merits of each case. However, in one of the great reversals of all time, just 14 years later, Congress again embraced mandatory prison sentences as part of then-President Ronald Reagan's renewed war on drugs.¹² The mandatory sentences were encoded in the Sentencing Reform Act of 1984, which denied even first-time drug offenders the promise of early parole.¹³ As a result of this new law, the prison system was soon overwhelmed with nonviolent first-time offenders serving lengthy mandatory sentences for drug-related convictions.

Through this confluence of historical forces, the United States has a greater percentage of its population in a jail or prison than any other country in the world (Zakaria, 2012). In contrast to the incarceration rate of 90 per 100,000 persons in Germany or the 96 per 100,000 persons in France, the United States has 760 prisoners per 100,000 people (Zakaria, 2012). Although the United States has just 5% of the world's population, this nation also holds the dubious honor of having 25% of the total number of people on earth who are incarcerated for one reason or another (Zakaria, 2012). If, as Hari (2015) observed, all of the people in the United States who are incarcerated were gathered together into one prison, it would be able to lay claim to the title of the thirty-fifth most populous state in the country. Four-fifths of these people are incarcerated for simple possession of an illegal compound (Zakaria, 2012).

An often-overlooked aspect of the criminal prosecution and incarceration of those convicted of drug-related offenses is that it is expensive to keep a person in prison. Zakaria (2012) reported that the cost of incarcerating one inmate in the California Department of Corrections was \$45,006 per year¹⁴ (Zakaria, 2012). If approximately 1.32 million of the people incarcerated in the United States are there simply for possession of a controlled substance, then this nation is spending \$59.4 billion dollars for the cost of incarcerating these people. Nor does the cost stop upon the inmate's

release from the penitentiary: Individuals who have been incarcerated earn 40% less than those who have never been incarcerated, thus reducing the amount of state and federal income taxes they pay, and increasing their subsequent dependence on state and federal supplementary funds for food stamps, etc. Individuals convicted of drug-related offenses are barred from state and federal tuition assistance programs for college or vocational-technical school costs, making it virtually impossible for the individual to train for a better job (McPherson, Yudko, Murray-Bridges et al., 2009). This after-incarceration punishment contributes to the high recidivism rate for drug offenders who are released from prison. In many cases, they are pushed back into a life of crime because they can do little else to earn enough money to support themselves or their families.

In retrospect, the Boggs Act and the Sentencing Reform Act of 1984 were both failures. In spite of widespread knowledge of the legal sanctions against illicit drug use, "millions of people every year join the legions who have experimented with illegal substances" (Phillips & Lawton, 2004, p. 33). For virtually every action there is an unexpected consequence, a truism that has become enshrined as the Law of Unintended Consequences. If you wish to "get tough on crime" by throwing first-time drug offenders into jail or prison, it will become necessary to release violent offenders from prison to make room for newly convicted drug offenders. As a result of this unintended consequence, the average sentence served by a person convicted of homicide is approximately 9 years, while a person convicted of growing 100 marijuana plants could be sent to prison for up to 40 years¹⁵ (Brust, 2004).

THE FORFEITURE FIASCO

During the administration of President Ronald Reagan, he pressured Congress to get "tough on crime" by enacting a series of "zero tolerance" statutes. The possession of *any* amount of an illegal substance was grounds for criminal prosecution under these statutes. People were prosecuted for offenses as innocuous as having money in their wallet tainted by traces of cocaine, as if this was proof of the individual's cocaine misuse. People found to have marijuana seeds in their car or boat were also vulnerable to prosecution. Only later was it shown that a significant percentage of the dollar bills in circulation were tainted by traces of cocaine simply by being rubbed up against another dollar bill that had traces of cocaine on it. It was also discovered that marijuana seeds blow in the wind. By then, however, the damage had been done, and numerous people had been prosecuted under the guise of zero tolerance.

Setting aside the constitutional provisions against unwarranted search and seizure, Congress also passed a law

¹² One has to wonder how many members of Congress voted in favor of these changes not because they thought that they might work, but because they were afraid of being accused of being "soft on crime" by their political rivals.

¹³ Parole from prison was once a privilege offered only to a few offenders who demonstrated exceptional efforts toward rehabilitation. Now it is expected, and is often viewed as a "right" of those being sentenced to prison. One will often hear the freshly convicted inmate state that although he was sentenced to prison for 10 years, for example, his parole date is only 3 years away.

¹⁴ A figure that includes the cost of salaries for the staff who work in the prison, the physical plant itself, construction costs, food, medical care, etc.

¹⁵ Which, if you consider that the offender was 25 at the time of conviction, is essentially a life sentence.

allowing law enforcement authorities to confiscate property on the simple *suspicion* that it had been purchased with money made from the illicit drug trade. Law enforcement agencies no longer had to *prove* that the property had been purchased with money made from the sale of illegal drugs. They only had to state their belief that this was the case. Not surprisingly, in the time since this law was passed it has been widely abused. Some police departments now *depend* on money and property seized under forfeiture laws for at least part of their operating budget. The level of abuse inherent in this law might be seen in the fact that up to 80% of the money seized by federal authorities comes from people who are *never* indicted for criminal activity, much less tried in a court of law and convicted (Leavitt, 2003). Police in at least two states (Florida and Louisiana) have been identified as using minor traffic offenses as justification to seize money from motorists who have committed no illegal act other than the traffic law violation because it *might* be drug money (Leavitt, 2003).

The forfeiture laws *do* carry a provision that allows the citizen whose property is seized to seek the return of the property. This process involves the individual filing a lawsuit against the agency that seized the property, then proving in court that he or she did not obtain the money or property from the illegal drug trade. This process is expensive, time-consuming, and the final cost of the process might be several times that of the property seized by authorities. Further, the agency that seized the property is not required to pay any form of interest on the material(s) seized. Few people are willing, or have the financial resources, to pay \$4,000 in court costs to prove that the \$1,000 they had in their wallet for a vacation trip when stopped by the police was rightfully theirs, for example.

As should be obvious by now, the social experiment of trying to eliminate the illicit drug trade through interdiction, incarceration, and punishment has been a failure. However, this does not stop law enforcement officials from trumpeting the minimal success of the past year, or from hinting that for just a few billion dollars more it might be possible to “win” the war on drugs. Unfortunately, law enforcement and incarceration of offenders, often touted as “a panacea for the problem of illicit drug use” (Fulde & Wodak, 2007, p. 334), has yet to prove effective. Indeed, the mandatory sentencing laws were intended to discourage upper- and middle-level dealers from engaging in drug distribution activities. However, these individuals are able to trade their knowledge for lighter prison sentences or even just probation! As a result of this process, only a minority of those incarcerated in the federal prison system were mid-level drug distributors, and more than half of those incarcerated are either individuals who misuse drugs or low-level dealers who sold drugs on the street corners.

4. Treatment¹⁶

The treatment of people who are not involved in the distribution or sale of illegal substances but who have a substance use disorder is a distant fourth when funds for the war on drugs are distributed. The total expenditure for drug rehabilitation is estimated to be \$15 billion from state and federal governments, and \$5 billion from insurance companies¹⁷ (Carey, 2008). Arguments that rehabilitation is not effective break down in the face of studies that have found that incarceration has been estimated to cost two to ten times as much as rehabilitation (Johnson, 2003). Other researchers have suggested that for every dollar invested in treatment, the community saves from \$4 to \$12 (Breithaupt, 2001; Brust, 2004; Dobbs, 2007; Mee-Lee, 2002; UKATT Research Team, 2009), up to possibly as much as \$50 (Garrett, 2000).¹⁸ These figures do not mean that treatment is appropriate for every offender convicted of a drug-related crime. In spite of the claims of advocates, “the addiction treatment field [has] not met either public expectations for reduction of addiction . . . or its own expectations to produce lasting abstinence” (McLellan, 2008, p. 94).

However, incarceration is also not the answer for every offender convicted of a substance-related crime. There should be an attempt to balance the application of legal sanctions against those of treatment, to find the appropriate response to the crime committed by each individual. In the year 2000, Portugal, for example, decriminalized drug use, placing the emphasis on education and rehabilitation. In spite of dire warnings, the removal of criminal sanctions against substance use has not resulted in a major increase in drug use. Indeed, there has been a slow but steady decline in drug use (Taverne, 2010). This would argue that legal sanctions against drug use are apparently not effective, a lesson that historians have known ever since the Prohibition era of the 1930s.

The Reality of the War on Drugs

Simply stated, the war on drugs is a failure (Hari, 2015; Zakaria, 2012). The worldwide effectiveness of this march of folly may be seen in the United Nations’ pledge in 1998 to win the war on drugs by the year 2008 (Room, 2009). The reality

¹⁶ Discussed in more detail in Chapter 30.

¹⁷ An amount that might increase now that the federal government has passed a “parity” law that requires that insurance companies reimburse for drug rehabilitation on an equal level as for other health problems.

¹⁸ These various estimates reflect, in part, different variables included from study to study. For example, one study might include long-term reductions in health care costs that another study does not include in its estimates of the savings that result from treatment.

is that the drugs (or at least those who market and use them) have won (“Winning the war on drugs?,” 2007). In its efforts to “win” this war, the United States has gone so far as to attempt to interfere with the internal affairs of other countries. One of many examples of this unwarranted, possibly illegal interference was seen in 2003, when the then “drug czar” of the United States accused Canada of trying to poison American youth by relaxing its internal marijuana possession laws (Reuter, 2009). This intrusion into the internal affairs of another country provides a fine example of how the weapons and tactics used in this “war” fail to work. For example, following the invasion of Afghanistan by U.S. armed forces, an estimated \$800 million a year was spent to eliminate the problem of illegal opium poppy cultivation in that country, without any apparent benefit (U.S. Special Envoy for Afghanistan and Pakistan Richard Holbrooke, quoted in Room, 2009).

In spite of the moralistic stance by those who argue against illicit drugs, the antidrug media campaigns launched with great fanfare, and attempts at interdiction by law enforcement agencies, the problem of illicit drug use has continued for over a century. In the name of protecting citizens from illicit drugs, constitutional rights have been ignored or circumvented. Citizens are criminally prosecuted to save them from the scourge of illicit drug use, which, according to the American Medical Association, is a disease.

The effectiveness of the war on drugs may be seen in the fact that in the early 1950s, when the population of the United States was around 151 million, only 60,000 people were estimated to be addicted to narcotics (Ropper & Brown, 2005). In the approximately 50 years after, the United States spent \$2.5 trillion dollars on the war on drugs (Fleming & Grey, 2008). Whereas one would expect that the number of those addicted to narcotics would double to 120,000 people based on the near doubling of the population (281 million in 2000), 1 million people in the United States were thought to be addicted to narcotics (Tinsley, 2005). As of 2015, over 2.5 million individuals have an opioid use disorder in the United States (Center for Behavioral Health Statistics and Quality, 2016), out of a population of almost 325 million people. These statistics hardly reflect a resounding success.

The failure of the war on drugs should not come as a surprise: We are fighting the war on multiple fronts: (a) collectively, we create the demand for illicit compounds, then (b) spend billions of dollars to interdict the compounds produced to meet this demand, and (c) spend even more money to prosecute those who use these compounds and are arrested. A survey by the Hazelden Foundation revealed that 79% of those people sampled believed that the war on drugs has not been effective (“Americans Want Insurance to Cover Addiction,” 2009). Interdiction efforts had been so “successful” that there were 66% more people addicted to hard core drugs

at the start of the 21st century than there were at the start of the last decade of the 20th century (Falco, 2005). Incarceration has also proven to be a magnificent success: In 1972, it was estimated that there were 200,000 jail and prison cells¹⁹ in the United States, and a quarter of a century later there were 2 million jail and prison cells in this country (Pepper, 2004). This war has waged on, in spite of the awareness that past legislative and legal efforts to control illicit substance use have all failed (McPherson, Yudko, Murray-Bridges et al., 2009). Rather than change a failed social policy, however, politicians have for a long time blindly follow the same path, hoping for a different outcome.²⁰ This reflects, in part, the tendency for politicians to ignore scientific evidence in favor of “pander[ing] to public prejudice” (Nutt, 2009, p. 5). Thankfully, there is potential change in the air, as the Western Hemisphere Drug Policy Commission Act, created by representatives from opposing parties, was signed into law in December 2016, though it is dependent now on the new administration of the United States (Gómez Romero, 2017). Gómez Romero hopes that the commission does focus on reducing the harm of current policies, with a true intention to create reform.

The Drug War as Political Nonsense

The analogy between the fairy tale “The Emperor’s New Clothes” and the war on drugs is striking. The program has been shown to be a dismal failure, but nobody wants to say this publicly. Perhaps this is because the war on drugs is designed to give the *illusion* that politicians are doing *something* about this social problem, without having to face reality: It is our *demand* for drugs that is the foundation for the illicit drug trade. As Delingpole (2009) noted, “in politics, unfortunately, fashion counts for rather more than integrity or ideology” (p. 9).

If politicians truly wanted to protect society from the dangers of substance use, they would address the most destructive compounds being used today: cigarettes and alcohol (the dangers of which have been discussed in previous chapters). However, the focus of the war on drugs is on those mind-altering agents that do not make a profit for the large corporations that can hire lobbyists (Rasmussen, 2008). Is it a coincidence that these industries also make lavish contributions to each political party on a regular basis? And consider the shifts in marijuana policies around medical and personal use. This is certainly not separate from lobbying efforts and political campaign contributions. Cocaine, heroin, and methamphetamine dealers

¹⁹ Jails are usually incarceration facilities at the county level. Prisons are incarceration facilities at either the state or federal level.

²⁰ One definition of insanity is doing the same thing over and over, hoping for a different outcome—which says something about the war on drugs, does it not?

generally do not make contributions to political parties in this country, and their products are, by coincidence, classified as illegal.²¹ It is not the purpose of this paragraph to argue that political contributions by what might loosely be called the alcohol and tobacco industries are wrong. This is the political system in which we live. However, it is the purpose of this paragraph (and the rest of this chapter) to make the reader question *why* the policies that are in place remain in place without question. A welcome voice of reason was offered by the U.S. Conference of Mayors, which publicly announced that the war on drugs was a failure (Curley, 2007). In the decade since then, slowly, other entities have also announced the failure, as the Global Commission on Drug Policy did in 2011.

Change is slow to happen. Sadly, it takes time for enough of the dissenting voices to be heard. “Dissenting voices must be suppressed” is the typical mindset, just as when Adolf Hitler first came to power in Germany of the 1930s. For example, the original draft of the Federal Omnibus Crime Bill called for people who criticized the federal government’s antidrug policies to be charged with *treason*, and for criminal prosecution for that offense (Leavitt, 2003). The chairperson of the United Kingdom’s Advisory Council on the Misuse of Drugs was dismissed in 2009 after voicing opinions that went counter to those of the government (“Drug disarray,” 2009). His “crime” was to point out that 1 of every 350 attempts to ride a horse resulted in a serious injury, while 1 of every 10,000 people who took MDMA suffered an adverse effect.

The War on Drugs as a Drain on National Resources

Remember that incarceration is one of the centerpieces of the war on drugs. Having caught the drug distributor or user, prosecuted the individual, and convicted him or her, the question becomes one of what to do next. Incarceration has been the answer, and it has been used with a vengeance: The expense of “treating” individuals with substance use disorders through the criminal justice system costs more than the SUD does to the individual, or to society (King, 2006).

An unintended consequence of the war on drugs is that the various states and communities became dependent on the salaries paid to those who staff the prisons built to house the influx of drug offenders. The same is true for construction companies contracted to build the new prisons. These agencies and states then have an incentive to maintain the war on drugs, thus also delaying the forces pushing for change. This is clearly seen in the repeated efforts of the Drug Enforcement Administration (DEA) to keep marijuana classified as a controlled substance. It has been said that the change in the

number of “illicit drug users” that would result from legalizing marijuana would make it hard for the DEA to justify its large budget to Congress (Walton, 2002). The vast majority of states and the District of Columbia have approved the use of medical marijuana at least for some indications, and a number of states have recently approved recreational use. The National Academies of Science, Engineering, and Medicine (2017) as well as the National Institute on Drug Abuse (NIDA; Volkow, 2017) are calling for further research on the benefits and risks of cannabis. Yet the DEA (2016a) stands strong in its position against removing marijuana from Schedule I, although they are moving toward allowing more research through creation of additional suppliers (other than the *one* supplier they approve) as well as potentially approving more entities to conduct the research.

Other Consequences of the Prohibition Against Drug Use

Medical sociologists have observed that, because of existing prohibitions against the use of illicit drugs, the individual who uses drugs must use his or her limited supply of drugs under hazardous conditions. Some of the consequences include an increased risk of death for those who use heroin (6–20 times higher than for the general population) (Drummer & Odell, 2001). Some of the causes of death for those who use intravenous drugs, for example, include drug overdose, infections (including HIV), malnutrition, accidents, homicide, and suicide. The medical treatment of those who use illicit drugs and then develop associated illnesses is an indirect part of the health care crisis in this country, as are the social supports necessary for the families of those who use illicit drugs.

An interesting social experiment involving the effort to address the illicit drug problem began in Portugal in 2001. The drug laws were revised so that they were less harsh, and punishments were made proportional to the crime. While the level of illicit drug use remained approximately the same, the demand on the health care system for substance-related illnesses and deaths dropped (Nutt, 2009). Further research found that since 2001, unlike the way street prices fell in the United States when harsher penalties were instituted, the street prices of drugs increased, which the researchers claim potentially lessens the likelihood of more people developing an SUD (Félix & Portugal, 2017). This is not to say that illicit drug use should be tolerated, but it does illustrate the consequences of the application of legal sanctions to address this social problem.

Section Summary

To date, each of the legs of the war on drugs has achieved at least a limited degree of success, but overall the program

²¹ There is a lesson here, but I am not the one who suggested it!

essentially has been a failure. The more successful interdiction efforts are, for example, the higher the profit margin for smugglers who succeed in bringing their product into this country, and the greater the incentive for others to enter the drug distribution or sales business. Thus, it has been impossible for society to arrest its way out of the drug use problem. While treatment holds some degree of promise, it is not the ultimate answer to the problem of drug use disorders sweeping across this country. Further, society does not address the issue that it is the demand for illicit drugs that fuels the “crisis” in illicit drug use. Thus, the war on drugs does not really address the basic problems in society that help to cause the problem, and those who openly call the war on drugs a failure are ignored, or their views are called unrealistic by those already committed to the same policies that have been shown to be such a dismal failure.

The Law and Morality: Where to Draw the Line?

In the modern war on drugs, federal and state authorities have applied legal sanctions against individuals who wish to use any of a long list of chemicals, or, in the case of alcohol, to use it beyond certain established limits. If, as the American Medical Association argues, the substance use disorders are disease states, then these legal sanctions essentially turn incidents involving those with SUDs into criminal acts. However, the law is selective: Only certain substances, or certain euphoric states, are deemed worthy of criminal prosecution (Husak, 2004). Those who use caffeine, for example, achieve a drug-induced psychological state without fear of arrest or incarceration. Long-distance runners achieve the “runner’s high” without fear of legal consequences (Husak, 2004). The individual who consumes alcohol, as long as she or he does not drive a motor vehicle while intoxicated or commit other crimes, can ingest alcohol to achieve a desired state of intoxication without fear of arrest.²²

In the 21st century, the line between legitimate medical purposes and recreational substance use has become rather uncertain. Some people will use a prescribed medication (take diazepam as an example) to achieve a desired mood state, but if another person were to take the same medication without a prescription to achieve the same mood state, he or she could be charged with a crime (Husak, 2004). Should this be the case? It has been argued that personal, recreational drug use

(as opposed to distribution of illicit chemicals to others) is a consensual crime. Are euphoric mood states grounds for legal sanctions? At what point does medical necessity blend into recreational drug use? If a man were to suffer from a clear case of erectile dysfunction, the prescribed use of a compound such as Viagra® would be appropriate. However, if a businessman were to ingest the same compound simply to enhance sexual performance, would this be grounds for criminal prosecution?²³ Both individuals may have obtained the compound by prescription from a licensed physician, but where is the line between legitimate medical need and recreational use of that compound? As Rasmussen observed,

the myth of a sharp divide between medical and nonmedical “recreational” drug use began to weaken. Some of the pharmaceuticals that people get from our modern medicine men suddenly began looking a lot like the illegal drugs that people take in alternative manners; perhaps some street “abusers” were actually self-medicating, and some legitimate patients were merely junkies hooked by the doctors and drug firms.

Rasmussen (2008, p. 175)

Imagine three hypothetical business executives. One will drink a martini to relax after a hard day’s work. The second will ingest a diazepam tablet for the same reason, while the third smokes marijuana at the end of the work day. The legal system tends to be exceptionally selective about where to draw the line, while failing to provide any rationale for this distinction. If a person were to use the wrong chemical to achieve a desired state of mind, he or she could be ruined by the legal consequences of that decision. Thus, the war on drugs might be viewed as a war on those who attempt to alter their state of consciousness in ways deemed inappropriate by segments of society. The understanding of this reality may have helped to begin the shift in the manner in which the United States attempts to deal with its drug use problem through referrals to treatment rather than incarceration (Fields, 2009).

The Debate over “Medical Marijuana”

It is ironic that the decision on whether “medical marijuana” should be allowed for the treatment of various medical

²²This assumes that the individual is not out on bond, probation, or parole. In many cases, probation or parole agreements stipulate that the individual must not ingest alcohol or illicit drugs as one of the conditions of the bond agreement, or of probation or parole. Consider once again, though, that these conditions may have been put on the individual in relation to previous contact with law enforcement because of illicit possession or use.

²³Before you answer this question, there is evidence that sexual performance enhancement compounds are commonly misused by college students for recreational purposes. Should they be prosecuted for “criminal” activity?

conditions rests upon a shaky foundation, because of the Drug Enforcement Administration's *a priori* decision that there were no compounds in marijuana of potential medicinal value. Thus, they saw no need to look for such potential pharmaceuticals, which has certainly greatly delayed our understanding of marijuana and its compounds.²⁴ Medical decisions²⁵ are being made at the ballot box rather than on the basis of sound research data, the result being that we lack research evidence about the efficacy or safety of medicinal marijuana at various dosage levels (Wade, 2015).

Through selective breeding, many different strains of marijuana have been developed with different levels of THC and other chemicals that naturally occur in the cannabis plant (Schatman, 2015). It is ironic that the Drug Enforcement Administration's long prohibition on research into possible medical applications of marijuana, or at least of a compound found in marijuana, has left it with a paucity of information to refute the claims of those who demand its use for compassionate reasons (“No dope on dope,” 2006; Schatman, 2015; Wilkinson, Cyril, & Souza, 2014). Marijuana continues to be classified as a Schedule I compound (Drug Enforcement Administration, 2016a).²⁶ despite many news outlets indicating that they would be moving it to Schedule II in 2016.

Unfortunately, we are in a climate in which the “current arguments for the use of medical cannabis are considerably more politically, and often emotionally, based rather than scientifically based, resulting in the proliferation of medical marijuana pseudoscience” (Schatman, 2015, p. 6). To adequately address the issue of medical marijuana, Schatman (2015) posed five essential questions: (1) Is medical marijuana safe? (2) Is there adequate evidence for its efficacy, and if so for what conditions? (3) If it is sold in dispensaries rather than on street corners, should it be considered “medical”? (4) If it is medical, can it still be misused? And finally, (5) if marijuana is used medically, do only certain compounds in marijuana have medical benefit, and are those compounds safe? To this list might be added a further question: (6) If marijuana or a compound in cannabis is found to have medical value, what are the optimal mode of administration and appropriate dosage?

²⁴ There is admittedly anecdotal evidence suggesting that a compound in marijuana might potentially curb or reverse the growth of tumors in the body (Casarett, 2015). As a person whose life is being cut short by a tumor, the author would like to thank the Drug Enforcement Administration's open-minded research into their *a priori* decision that since they recognize no medicinal value in *any* compound in marijuana, there is no reason to look into this possibility. Such reasoning would have also deprived us of digitalis and a host of other pharmaceuticals originally used by local healers to treat disease, since the reports of their effectiveness were only anecdotal.

²⁵ What conditions medical marijuana should be used to treat and how often the patient should be able to use the marijuana to treat this condition, for example.

²⁶ See Appendix 3.

Because of the lack of a standard list of medical conditions for which marijuana might be prescribed, as these vary from state to state if such usage is even legal, training programs for physicians who wish to utilize marijuana as an adjunct to standard treatments for other disorders have only recently been created. Detractors of the proposed use of marijuana as an adjunctive agent in the treatment of various medical disorders suggest that allowing such initiatives to pass will encourage marijuana misuse. This belief is not supported by clinical evidence, which suggests the opposite: Authorizing the prescribed use of marijuana might reduce its attractiveness to those who misuse the substance (Gorman & Huber, 2007). As this would suggest, the use of marijuana for medical purposes is a process that is still evolving, with future research holding the potential for great gains in the treatment of disease or great disappointment if anecdotal stories end up unsupported by objective clinical research.

It must be emphasized that the medicinal use of marijuana is not the same as the *legalization* of marijuana, although public perception often holds that they are the same. The medicalization of marijuana would simply place it on an equal footing with other accepted pharmaceuticals and allow researchers to identify components in marijuana that might be of value to health care professionals. As is true today for the other pharmaceuticals, the possession of any of these compounds without a prescription would be grounds for legal prosecution. The relationship between medicalization and legalization might best be viewed as illustrated in Figure 38-1.

Unfortunately, the federal government has maintained the stance that even doing basic research into possible medical applications of marijuana is illegal in most instances. The American Medical Association has argued that marijuana should be reclassified as a Schedule II compound, which would then researchers to explore potential applications for the various chemicals found in marijuana smoke. However, as

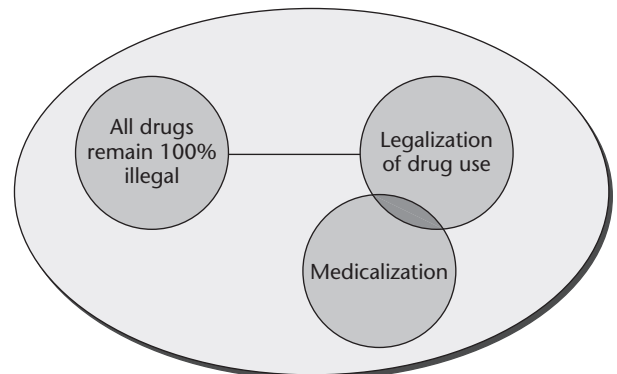


FIGURE 38-1 Medicalization and Legalization as Two Different Concepts.

of the writing of this chapter, marijuana remains a Schedule I compound, and this decision is defended on the ground that (a) there are no *proven* uses for marijuana, so (b) there is no need for research to identify a legitimate application for marijuana in this country. In the last decade, the DEA has threatened to suspend a physician's license to write prescriptions for supposedly writing prescriptions for certain illicit compounds, but the courts ruled that this was a violation of the physician's First Amendment rights (Hoffmann & Weber, 2010). Yet recently, the DEA and the Colorado Medical Board have suspended doctors based on recommendations for medical marijuana that are beyond the typical amount allowed (Ingold, 2017). This is a complex issue, and the debate over the use of marijuana for medicinal purposes will continue well into the 21st century.

In response to citizen initiatives, a number of different states have legalized the medical use of marijuana after contentious debates and political initiatives that often place the laws of various states at odds with federal law, starting with California in 1996. Almost all states allow at a minimum some limited access to some medical marijuana (Gruber & Sagar, 2017). To avoid controversy, a number of legislative districts have also placed enforcement of marijuana possession laws at the bottom of their priority list (Caulkins et al., 2015), while other states have begun to reduce penalties for recreational use of marijuana (Ryan & Ammerman, 2017), both shifts that in essence give tacit permission for possession of small amounts of marijuana for personal use. The ultimate status of marijuana and what medicinal benefits might be found in one or more compounds contained in this plant are still uncertain, though it is safe to say that marijuana use will remain controversial for many years to come.

Cannabidiol (CBD) and Other Compounds in Cannabis

For medical purposes, marijuana is given as a pharmaceutical preparation or through oils, leaves, and also through things that can be eaten or drunk (Ryan & Ammerman, 2017). As the reader might recall, CBD is one of the compounds found in marijuana, and it is intended to be passed to the individual through these varieties of preparations. However, there seems to be an inverse relationship within current strains of cannabis, with those strains bred to have the highest levels of THC having the lowest levels of CBD. This is unfortunate, as early research studies suggest that many of the bodily changes currently thought to be of medical value in marijuana might be caused by CBD and not THC. As of early 2017, the Health and Medicine Division of the National Academies of Science concluded that, although more research is needed in all areas, there is strong evidence for cannabis or cannabinoid use

to treat chronic pain in adult patients, some symptomology experienced by those with multiple sclerosis (MS), and for nausea and vomiting in chemotherapy patients. They found some evidence of an extract of cannabis as helpful in treating short-term sleep issues with some individuals with other medical disorders (such as MS, chronic pain). There is a need for further research on a substantial number of additional uses, with limited or no support as of yet for effectiveness (for instance, with epilepsy; National Academies, 2017). However, negative effects have also been found related to the cannabinoids, such as difficulty concentrating or thinking clearly, dizziness, and a strong sense of uneasiness or dissatisfaction with life (Ryan & Ammerman, 2017).

In their attempt to alleviate if not cure illness, physicians find that patient noncompliance with prescribed medications is a significant problem.²⁷ This noncompliance is often due to the individual's inability to tolerate the side effects of prescribed medications. To date, researchers have found that CBD is well tolerated, and no cognitive or sensorimotor side effects have been identified. Although systematic research studies are lacking at this time, there is evidence that CBD might serve as a useful adjunctive medication in the treatment of various disorders. As this suggests, CBD demonstrates some potential as a pharmaceutical, yet there is a need for further research into its effects and the most effective dosage levels if it is found to have medicinal value as either a monotherapeutic agent or an adjunct to other existing medications. It is ironic that in the rush to authorize the medical use of marijuana, many states may have legalized the medical use of marijuana before proper studies were carried out to determine which compounds might have medicinal potential in marijuana and how they might best be used.

Legalization of Marijuana

Should marijuana be legalized? We are seeing a move in that direction, given that as of the 2016 elections, eight states and the District of Columbia have legalized the possession of small amounts of marijuana. In the Netherlands, marijuana use is generally accepted, and the individual is allowed to have small amounts of marijuana for personal use if it was purchased in a government-approved coffeehouse. There is a tax placed on marijuana, providing a source of revenue. Illicit drug distributors are still subject to arrest and prosecution, however. Thus, the government-sanctioned use of marijuana is within strict limits, and the laws of the country are still applied to those who sell and distribute illicit marijuana.

²⁷ Discussed in Chapter 34.

Despite some of the most draconian of legal measures, marijuana use has not been eradicated in the past half century; arguably, the campaign has made marijuana use even more attractive as a drug to misuse *because* it has been and in many places continues to be illegal. Since the mid-1980s, support for the legalization of marijuana has been increasing, with recent research indicating that the majority of people in the United States will support legalization within the next 10 years (Campbell, Twenge, & Carter, 2017). In Colorado, the first state to legalize possession of small amounts of marijuana, use has not increased since legalization (Ghosh et al., 2017). This research is the first of many that proponents of legalization hope will continue to show that legalization is actually helpful, or at least less harmful to society than are current legal sanctions.

Proponents of the legalization of marijuana point out that legalization, even with strict controls such as those put into place in the Netherlands, would remove a source of income from what is loosely called “organized crime.”²⁸ The appropriate taxes might serve as a source of an additional \$33 billion a year in revenue for the government, which is hardly an insignificant matter²⁹ (Cafferty, 2009). While there is a danger that legal access to marijuana might contribute to the potential adverse consequences inherent in marijuana use, one must ask whether these consequences are less costly, both financially and in terms of human lives, than the current measures imposed on those who are arrested because of marijuana use.

Arguably, marijuana may be slowly losing its appeal among adolescents and young adults, many of whom use the compound as a form of rebellion. It has been argued that “if the appeal of drugs lies in their prohibited status, then we must expect that cannabis will soon be as fascinating as a new set of tax guidelines [if decriminalized]” (Walton, 2002, p. 137). The author did admit that there might be a short-term increase in the number of marijuana users, but as time passed the number of users would probably decline among the many who are drawn to it now simply because it is illegal. The research on Colorado and future results from states that recently approved marijuana possession in small amounts will help determine the accuracy of these assumptions. In Portugal, antidrug laws were repealed or drastically revised in 2001, and that country

has seen a decrease in consumption of drugs overall in the past 15 years (Cabral, 2017). The legalization of at least marijuana has also been tried in various other countries in Europe with some success. However, those who set policy at the federal level in this country have thus far turned a blind eye to these social experiments, continuously reaffirming their belief in the failed policy of legal repression.

Chapter Summary

Historically, the war on drugs is based on four legs: (a) elimination of illicit compounds through destruction of raw materials, (b) interdiction of drugs being shipped to this country, (c) legal sanctions against those who engage in the use of the substances deemed illegal by the government, and apparently if all else fails (d) treatment of those addicted to these compounds. These policies have failed miserably in spite of the expenditure of trillions of dollars.

Future historians may well conclude that the only groups to benefit from the war on drugs are (1) those involved in the illicit drug trade, (2) street gangs involved in the daily distribution of the drugs and who profit from their sale, (3) the government employees whose jobs depend on the war on drugs, (4) politicians who talk about “getting tough” on crime by stamping down on those who use illicit drugs, (5) construction company employees whose jobs depend on building the prisons to house those convicted of drug-related offenses, (6) people hired to staff the aforementioned prisons, (7) various police departments that have come to be dependent on federal and state subsidies to fight the war on drugs, and (8) terrorist groups that benefit from the sale of illegal drugs to fund their own activities.

The question of whether an illegal drug(s) should be legalized, and under what conditions, is a social issue, not a medical one (Brust, 2004). There are many who argue that society should blindly “stay the course,” even if that course is toward the shoals of financial ruin and social upheaval. The last half century has demonstrated that society cannot arrest its way out of the current situation. Can society then provide enough treatment beds for those with substance use disorders?³⁰ There are no clear answers, nor is it clear which new social policies will be effective in addressing this social dilemma. However, as has been demonstrated in this chapter, there is a need for a long, *honest* examination of existing policies to identify those that work and those that should either be modified or dismantled.

²⁸ A biochemist who agreed to be interviewed only if the pseudonym “Dr. K.” was used offered a rather unique suggestion: Legal compounds that might differ from illicit drugs by only a molecule or two but that allow the user to get high should be legalized. This would have the effect of financially crippling the drug cartels, in addition to offering the user a legal substance to use to get high (Slezak, 2014).

²⁹ Or, given the casual manner in which politicians in Washington toss around budgets of *trillions* of dollars, perhaps this figure is meaningless.

³⁰ This statement assumes (a) that effective treatment methods can be developed that have (b) a minimal risk of relapse, a complication of substance rehabilitation programs that only complicates matters a hundredfold.

Are alcohol and the illicit drugs “evil”? Individuals’ responses to this question are based on their perspective. The perspective is based both on personal experience and social feedback. To use an analogy, is a knife evil? Knives have been in use for thousands of years. If a person were to use a knife to slice a Thanksgiving turkey, is that an evil act? If that person were to use a knife to commit a murder,³¹ is the knife an evil thing? It is important to remember that knives, alcohol, and drugs are inanimate: *It is the manner in which they are used* that determines whether an object is helpful or harmful. As a topical anesthetic, for example, cocaine might bring welcome relief from an injury, whereas other uses may be deemed physically harmful to the individual.

³¹“Jack the Ripper” comes to mind here.

In neither case is the chemical itself evil. It is the purpose for which the compound is used that society uses to classify it. The standards society uses to make these judgments are subject to religious sanctions, legal regulations, information (and misinformation), political pressures, etc. The antidepressant medication fluoxetine and the hallucinogen MDMA both cause select neurons in the brain to release the neurotransmitter serotonin and then block its reabsorption. Yet one is a recognized and accepted pharmaceutical, while the other is illegal.³²

³²The same point might be made about drugs used to treat erectile dysfunction. A small but significant percentage of those who use such drugs do so not because they suffer from some degree of impotence, but because they find that it enhances sexual performance. Is this appropriate, or it is a form of medication misuse?

The *Diagnostic and Statistical Manual of Mental Disorders* (5th Edition) (DSM-5) and Substance Use Disorders¹

The *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (DSM-5) (American Psychiatric Association, 2013) departs from the classification system used in earlier incarnations of the *Diagnostic and Statistical Manual of Mental Disorders* in a number of ways. First, in a format change similar to that made in earlier editions of this text, in the DSM-5 the words “dependence” or “addiction” are no longer used as modifiers following the name of the substance being abused. Rather, the more generic term “[insert name of drug of misuse here] use disorder” is used (for example, “alcohol use disorder” rather than “alcohol dependence”). The term *substance use disorder* avoids the stigma associated with terms such as “alcoholic” or the slightly less pejorative term “alcohol-dependent” (for example). Unfortunately, one unintended effect of this semantic change is that it is not clear from the phrase **alcohol use disorder** whether alcohol *abuse* or *dependence* is being discussed.

Two welcome changes to the DSM-5 are noted. The first is that the modifier “in a controlled environment” is now available for the clinician to use for cases in which a person might claim to have been abstinent from a compound(s) for a certain period of time but fails to mention that they were in an environment (for example, under strict parole supervision with frequent urine toxicology tests or a prison) where access to alcohol or drugs of abuse was limited at best. The author of this text has spoken with many clinicians in the field of substance abuse rehabilitation who expressed irritation with persons who claimed to have been “clean” from alcohol or drug(s) for a certain period of time only to later find that they were incarcerated for much or all of their “clean” time. It is one thing to be abstinent from alcohol or drugs by choice.

It is a far different thing to be abstinent from alcohol or drugs because they were rarely (if ever) available to use. Further, the author of our text has spoken with a large number of former inmates who insisted that they intentionally abstained from alcohol or drugs while incarcerated to avoid the risk of making themselves vulnerable to predatory inmates.

The DSM-5 does address *substance-induced disorders*, such as the various withdrawal syndromes that develop when a person discontinues the use of a drug of abuse. This category would also include cases where the person’s use of a substance either caused a disorder that appeared to be a more traditional psychiatric illness (for example, depression that develops during withdrawal from cocaine or the amphetamines). Upon completion of the cocaine withdrawal process, the individual’s depression might resolve, or become less intense, revealing how their abuse of cocaine contributed to the development of a severe depressive reaction.

A characteristic that the DSM-5 shares with earlier versions of the manual is the identification of those individuals who are in *early remission* as opposed to those who are in *sustained remission*. The DSM-5 also allows the assessor to specify whether a client is in a treatment program (such as a methadone maintenance program for opioid addiction) as well as the circumstances under which the individual might be abstinent from drugs of misuse. This should also serve as a warning to the assessor that the individual might be misusing other drugs if they are unable to obtain their desired drug. It is not uncommon for persons whose opioid use is controlled through the use of an opioid agonist such as methadone to start to misuse other compounds (“switching addictions”) in an attempt to find another way to achieve the same substance-induced euphoria.

The DSM-5 notes that the diagnosis of a substance use disorder rests on four legs: (a) *impaired control*, (b) *social impairment*, (c) *risky use*, and (d) pharmacological characteristics

¹The summary of the information in DSM-5 provided in this appendix is provided for illustrative purposes only and should not be interpreted as nor function as a guide to patient care.

of substances being abused. These criteria are similar to those found in other books on the substance use disorders. The reader will note that the author of this text did not list the exact diagnostic criteria identified by the *DSM-5* as being necessary for a diagnosis of a substance use disorder. To do so would be repetitious, since many of the criteria apply to different drugs of misuse (development of tolerance is a common denominator for addiction to drugs of misuse, for example). Also, the criteria along with their definitions are already listed in the *DSM-5*, and it would make this text at least twice as long (and twice as expensive) to repeat information available in the *DSM-5*.

Although the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (*DSM-5*) (American Psychiatric Association, 2013) was introduced with great fanfare, it has generated significant controversy. Individuals on the various subcommittees charged with reviewing different sections of the previous edition of the *Diagnostic and Statistical Manual of Mental Disorders* were required to sign nondisclosure statements, in effect placing a “gag order” on what should have been an open exchange of ideas between mental health professionals during the development of this document (Greenberg, 2013). At least one member of the staff charged with the development of *DSM-5* quit, critical letters were submitted to various professional journals prior to its publication, and many news stories critical of *DSM-5* were reviewed in the mass media. Many critics of the *DSM-5* pointed out that the wording of terms used to define various psychiatric disorders is so vague that upwards of 20% of the population could be diagnosed as having a psychiatric disorder. Further, the definitions used in the text are frequently changed (diagnostic categories) (Ropper, Samuels, & Klein, 2014). What might have been viewed as an idiosyncrasy or personality quirk would be, under the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (*DSM-5*) (American Psychiatric Association, 2013), now a psychiatric disorder (Frances, 2013).

Further, arbitrary decisions to change inclusion criteria for psychiatric conditions were made without a statistical research foundation for these decisions. For example, the period of normal mourning following the loss of a close relative

was changed from 6 months as identified in the previous edition of the *Diagnostic and Statistical Manual of Mental Disorders* to just two weeks. After this two-week period, the individual would be classified as having a major depression (Greenberg, 2013). The criteria for a diagnosis of a substance use disorder were drastically revised, with the result that many persons who would previously not have met the criteria for a diagnosis of alcohol abuse or dependence would now receive such a diagnosis, with potentially lifelong consequences.

Critics of the *DSM-5* program have expressed a fear that the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (American Psychiatric Association, 2013) allowed individuals on the various subcommittees to insert conditions of personal interest into the diagnostic nomenclature without statistical evidence suggesting that the recommended category was a new psychiatric disorder. It was observed that more than half of the psychiatrists involved in the development of the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (American Psychiatric Association, 2013) had ties to major pharmaceutical companies² (Frances, 2013). Detractors observe that each diagnostic category in the *Diagnostic and Statistical Manual of Mental Disorders* (5th edition) (American Psychiatric Association, 2013) was reviewed in the ninth edition of the World Health Organization's *International Classification of Disease* (ICD-9) manual (the eleventh edition is currently pending). The *DSM-5* manual openly refers to how conditions that were diagnosable under *DSM-5* were classified in the ICD-9 system as an aid to the psychiatrist, raising questions as to why the *DSM-5* was necessary. Finally, the authors of the *DSM-5* appear to have forgotten that the various disorders included in the manual are just *constructs* developed by psychiatrists to quickly communicate essential information about a client to each other (Greenberg, 2013). These constructs do not exist in reality any more than there are IQ points running around our feet.

²By coincidence, many of these pharmaceutical companies just happen to make medications purported to treat these disorders.

APPENDIX 2

Drug Classification Schedules

The Comprehensive Drug Abuse Prevention and Control Act of 1970 provided for the classification of all compounds into one of five categories, depending on their misuse potential and medical applications. It is one of the most confusing aspects of drug rehabilitation work for health care and drug rehabilitation professionals. It is also the system by which drugs are identified for legal prosecution. This classification system is based not on the pharmacological properties of a compound, but on its perceived misuse potential, and, as noted, all pharmaceuticals are classified as falling into one of five categories by the Drug Enforcement Administration (DEA, 2017; McPherson, Yudko, Murray-Bridges, Rodriguez, & Lindo-Moulds, 2009):

Schedule	Definition and Examples
Schedule I compounds	Compounds with no recognized medical use. Examples: marijuana, LSD, MDMA, heroin
Schedule II compounds	Compounds with a recognized medical use, but with a very high abuse potential. Examples: morphine, amphetamine compounds
Schedule III compounds	Compounds with recognized medical use, but with a moderate abuse potential. Examples: ketamine, codeine
Schedule IV compounds	Compounds with recognized medical use, but with a mild abuse potential. Examples: phenobarbital, benzodiazepine compounds
Schedule V compounds	Compounds with recognized medical use, but with a low abuse potential. Example: lyrica

The Twelve Steps of Alcoholics Anonymous¹

Step One: We admitted that we were powerless over alcohol—that our lives had become unmanageable.

Step Two: [We] came to believe that a power great than ourselves could restore us to sanity.

Step Three: Made a decision to turn our will and our lives over to the care of God *as we understood him*.

Step Four: Made a searching and fearless moral inventory of ourselves.

Step Five: Admitted to God, to ourselves, and to another human being the exact nature of our wrongs.

Step Six: Were entirely ready to have God remove all these defects of character.

Step Seven: Humbly asked Him to remove our shortcomings.

Step Eight: Made a list of all persons we had harmed, and became willing to make amends to them all.

Step Nine: Made direct amends to such people wherever possible, except where to do so would injure them or others.

Step Ten: Continued to take personal inventory and when we were wrong, promptly admitted it.

Step Eleven: Sought through prayer and meditation to improve our conscious contact with God *as we understood him*, praying only for knowledge of His will for us, and the power to carry that out.

Step Twelve: Having had a spiritual awakening as a result of these steps, we tried to carry this message to alcoholics and to practice these principles in all our affairs.

¹Reproduced with the kind permission of Alcoholics Anonymous World Services, Inc.

The “Jellinek” Chart for Alcoholism

Following the publication of earlier editions of *Concepts of Chemical Dependency*, questions were raised concerning my decision not to mention the so-called Jellinek chart in this text. This chart, which is viewed as gospel within the alcohol/drug rehabilitation industry, purports to show the progression from social drinking to alcoholism, then on to recovery. Since the time of its introduction, the chart has been used to illustrate the “unalterable” progression of alcoholism to countless patients who were in the earlier stages of alcohol use problems, as well as to browbeat reluctant individuals into accepting the need for help with their supposed drinking problem. Variations of the chart have been developed for compulsive gambling, steroid abuse, compulsive spending, both heroin and cocaine addiction, and countless other disorders. An example of this chart is shown in Figure A4-1.

The problem is that Jellinek did *not* devise this chart! Though it is often attributed to Jellinek, the chart is actually the work of Dr. Maxwell Glatt, a British physician who was so taken by Jellinek’s work that he operationalized the gamma subtype of alcoholism in chart form. The chart, which addresses *only* the gamma subtype of alcoholism as suggested by Jellinek (1960), has mistakenly been accepted by countless alcohol and drug rehabilitation professionals as *the* chart that identifies the progression of *all* forms of alcoholism. As a result of this mistake, many patients in rehabilitation programs, whose symptoms of alcohol use problems did not “fit” the progression of symptoms suggested in the chart, have been subjected to countless hours of confrontation because they were “in denial.” Rather than perpetuate this misunderstanding, I decided not to make any reference to this chart in the text of *Concepts of Chemical Dependency*.

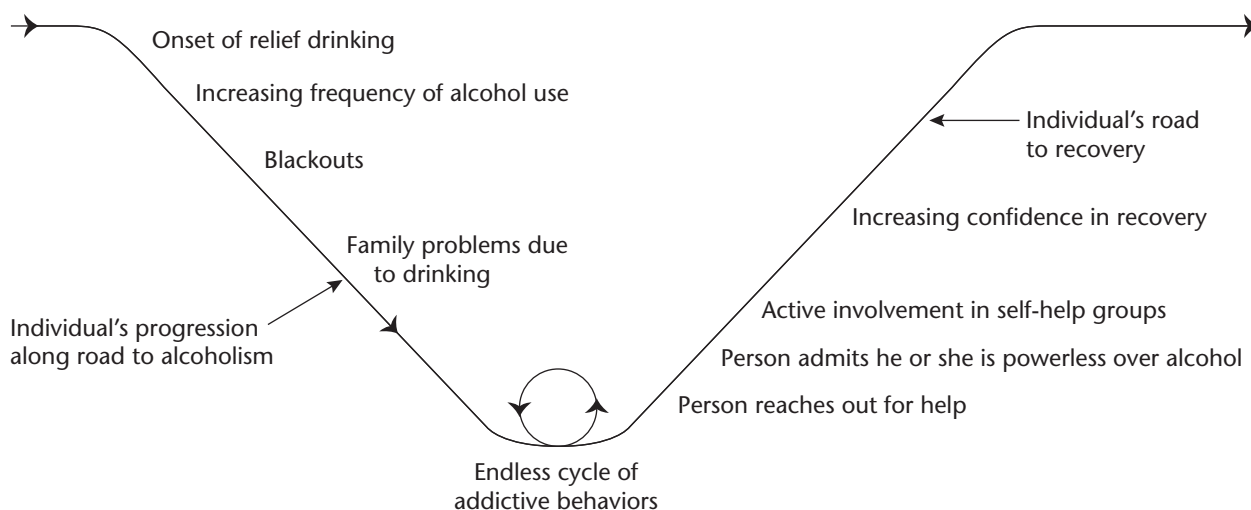


FIGURE A4-1 Alcohol Progression Chart Often Mistakenly Called the “Jellinek” Chart.

Glossary

- Acetaldehyde** Toxic compound, possibly carcinogenic, that is produced during the process of alcohol biotransformation and cigarette smoking. The biotransformation of acetaldehyde is blocked by disulfiram, making the individual who has consumed alcohol feel ill, which in theory should reduce the desire to drink.
- Acetylcholine** One of the major excitatory neurotransmitters. Acetylcholine activates muscle cells in response to motor activation commands from the brain, and is also involved in anger, aggression, and sexual behaviors.
- Acquired tolerance** Adaptive changes within the neurons which results in a tolerance to the presence of narcotic (or other substance) molecules.
- Action stage** Stage during which the individual takes concrete steps to modify identified problem behavior(s).
- Activities of daily living (ADLs)** There are two types of ADLs. The basic ADLs include basic activities such as grooming, getting dressed, feeding, bathing, etc. *Instrumental ADLs* involve more complex tasks such as money management, shopping, medication management, and being able to arrange for transportation as needed.
- Acute aortic dissection** See: *aortic dissection*.
- Acute coronary syndrome** Any condition brought on by sudden, reduced blood flow to the heart.
- Adenylate cyclase** An enzyme involved in the process of transmission of pain messages in the central nervous system, which may be inhibited by marijuana use.
- Adipose tissue** Fat tissue.
- ADHD** See: *attention deficit hyperactivity disorder*.
- ADLs** Abbreviation for *activities of daily living*. There are two types of ADLs. The basic ADLs include basic activities such as grooming, getting dressed, feeding, bathing, etc. *Instrumental ADLs* involve more complex tasks such as money management, shopping, medication management, and being able to arrange for transportation as needed.
- Agensis** Failure of development in, or damage to, a specific body organ during prenatal development.
- Agonist** A compound that activates a receptor site by being able to mimic or enhance the actions of a natural neurotransmitter.
- Agranulocytosis** A condition in which there is an insufficient number of white blood cells (called neutrophils or granulocytes), which results when white blood cells are destroyed more rapidly than they are produced.
- Albumin** One of the primary protein molecules found in the general circulation.
- Alcohol flush reaction** A reaction in certain individuals that is the result of a genetic mutation that prevents the liver from being able to produce sufficient amounts of aldehyde dehydrogenase, thus allowing high levels of acetaldehyde to accumulate in the person's blood.
- Alcohol-induced gastritis** A painful condition in which the stomach becomes inflamed.
- Alcohol intoxication** When drinking alcohol has resulted in a state of intoxication.
- Alcohol use disorder** A term that is applied to individuals whose use of alcohol is far in excess of the norms for his/her social or cultural group. This term is slowly gaining popularity over the older terms *alcohol abuse* and *alcoholism*, in part because it is more inclusive, and it lacks the social stigma of these other terms.
- Alcohol withdrawal syndrome (AWS)** A group of symptoms that occur after discontinuation of alcohol, particularly in those who have a physical dependence on alcohol.
- Alcoholic hallucinosis** The experience of hallucinations during alcohol withdrawal.
- Alcoholic hepatitis** Condition which is an extension of steatosis, with the additional symptoms of liver inflammation, pain, the death of liver cells, and development of collagen deposits in the liver.
- Aldehyde dehydrogenase** The family of enzymes that the body produces to rapidly break acetaldehyde down into acetic acid.
- Allele** A variation of a gene.
- Allodynia** Condition resulting from pain recognition system neurons responding to normal stimuli as if such were a sign of injury, sending pain messages to the brain when there is no injury.
- Alpha half-life** Period following peak concentration of the drug in the blood and when it is redistributed to various blood tissues.
- Alveolar** Pertaining to the little pockets in the lungs where the process of oxygen/carbon dioxide exchange is carried out.
- Amblyopia** Loss of vision or decrease in vision, often referred to as "lazy eye."
- Amnesia** See: *retrograde amnesia* or *anterograde amnesia*.
- Amygdala** A region in the brain that is shaped like an almond, located in each temporal lobe. This region is thought to be involved in the process of attaching emotional context to memory and modulating emotional responses to external reality. This includes behaviors centered on the process of obtaining reward(s), and the anxiety and panic responses.

Analog, drug A chemical that is a variation of the chemical structure of another compound, producing a “new” drug. The original compound is known as the *parent* compound, while the variation is known as an *analog* of the parent compound.

Anaphylactic shock Severe, potentially fatal whole-body allergic reaction to a chemical that the body views as an allergen. Various tissues in the body release massive amounts of histamine, triggering the allergic reaction cascade. Some of the symptoms of anaphylactic shock include rapid swelling of the mouth and throat, causing the airway to constrict (and possibly close entirely), chest discomfort, hives, loss of consciousness, cardiac arrhythmias, and potential death.

Angina Pain in the heart caused by the muscle tissue of the heart suffering damage through a reduction in blood flow to the tissue.

Anhedonia Inability of a person to take pleasure in activities that s/he once enjoyed. This condition is a feature of some personality disorders, major depression, schizophrenia, and is seen in the withdrawal syndrome from various drugs of abuse.

Anorexia Loss of desire to eat for an extended period of time, thus resulting in weight loss.

Anorexic Causing a state of anorexia.

Antagonist A compound that is able to fit into a receptor site *without* activating it.

Anterograde amnesia Inability to remember events after a specific point in time. This condition usually results from any of a wide range of forms of neurological trauma, or a wide range of chemical compounds.

Alcohol-induced “blackouts” are a form of chemically induced state of anterograde amnesia. Other medications, such as Versed, a benzodiazepine often used in “conscious sedation” medical procedures, and ketamine also can induce this same effect.

Traumatic brain injury may also induce anterograde amnesia. It is not uncommon for a patient who has been in a motor vehicle accident to assert that they cannot remember events for the first few hours or days after the accident. It should be pointed out that anterograde and retrograde amnesia are not mutually exclusive, and may coexist in the same patient.

Anticipatory guidance Helping a client to anticipate that a certain experience might happen, in order to mentally prepare for such a possibility.

Antidipsotrophic An obsolete term used to identify compounds that would combat dipsomania, or chronic alcohol use.

Antipyretic Against fever.

Antisocial personality disorder Disorder characterized by inflexible pattern of manipulating/exploiting others, including possibly violating others’ rights, which shows a significant impact on relationships with others on a long-term basis.

Antitussive Agent used to control cough.

Anxiolytic A compound that reduces the individual’s subjective anxiety level. This term is rapidly growing in acceptance over the older term “minor tranquilizer.” A confounding problem is that low doses of hypnotic drugs often are used to control anxiety, while higher doses of the same medications induce sleep.

A compound’s anxiolytic effects appear to reflect its actions on the limbic system of the brain, while the hypnotic effects of the same drug appear to reflect its effects on the cortex of the brain (Lehne, 2013). This rule is true for both the barbiturates and the newer benzodiazepines (Lehne, 2013).

Aortic dissection A phenomenon in which the inner layer of the aorta separates from the outer layers. With each heartbeat blood is forced into the dissection, forcing the tissues to rip apart even further. This condition is a surgical emergency and is frequently fatal.

Arteritis Inflammation of an artery.

Aspirative pneumonia A form of pneumonia that results when the individual aspirates stomach contents into the lungs during the process of vomiting. Bartlett (1999) identified two necessary components: (a) the aspiration of stomach contents into the lungs as a result of a breakdown of normal body defenses designed to prevent this, and (b) damage to lung tissue from gastric juices or bacterial infection.

Assessment Process used to determine the specifics related to a certain disease or condition for an individual.

Astrocytes A form of glial cell in the brain, which helps to provide physical support to the structure of the brain, as well as possibly playing a role in the transfer of molecules from the blood to the neurons of the CNS.

Ataxia Inability to properly coordinate muscle movements.

Attachment bonds Ties to others that initially begin with parents or caregivers, and expand over time to a broader sphere of people.

Attention deficit hyperactivity disorder (ADHD) Behavioral disorder in which the individual lacks the ability to focus attention on the task at hand. There are two subtypes: the *inattentive* variety, and the *hyperactive* variety. The latter is more often diagnosed, since children with this disorder are more likely to be recognized. It has been estimated that 3% of children with ADHD will “mature out” of this condition each year, the result being that for many individuals ADHD continues well into adulthood.

Saul (2014) argues persuasively that ADHD is frequently misdiagnosed. In his work he discusses a number of conditions that can produce ADHD-like behaviors in children that are rarely considered when a health care professional is making the differential diagnosis. If the cause of these ADHD-like behaviors is misdiagnosed, the treatment is likely to be ineffective. In his book he argues that the diagnosis of ADHD should be one of exclusion, in which these other conditions are ruled out before the possibility of attention deficit hyperactivity disorder is considered.

AUD Abbreviation for *alcohol use disorder*.

Auto-amputation A phenomenon in which the body essentially blocks the circulation to a limb so that the tissue dies. In the case of a limb, it will actually fall off. This is seen in cases of severe trauma, infection, or as a side effect of some chemicals.

Autonomous motivation When an individual requests treatment solely on his or her own motivation.

Bagging When a compound is poured into a plastic bag and then inhaled by the individual, placing the bag over the mouth and nose to inhale the concentrated fumes.

Barrett’s esophagus A condition that develops after the esophageal tissues have been repeatedly exposed to digestive juices during gastric reflux, as well as a possible traumatic rupture of the esophagus.

Benzodiazepine receptor agonists (BRAs, Z-compounds) A newer class of medications that are often used instead of benzodiazepines due to their lower misuse potential.

Beta half-life The decline in the plasma concentration as a drug is biotransformed and eliminated from the body.

Bibliotherapy Use of assigned readings to help the client better understand different concepts presented in individual or group therapy sessions.

Bioavailability Concentration of an unchanged chemical at the site of action.

Biofeedback Process in which the individual is provided real-time information about internal body functions such as brain wave or skin resistance patterns.

- Bipolar affective disorders** Disorders characterized by mood swings, such as mania, hypomania, and depression, that significantly impact daily living.
- Black market** System through which products are obtained outside of normal channels and then sold for profit to those who are willing to pay for them.
- Blackout** The condition resulting from consuming sufficient quantities of alcohol, which then interferes with the formation of memories in the individual's brain.
- Blood alcohol level (BAL)** Measurement of the alcohol concentration in the person's blood or exhaled breath.
- Blood-brain barrier (BBB)** A structural component of blood vessels in the brain that blocks the passage of many toxins, bacteria, and other substances that might cause harm to the brain.
- Body packer** Individual who will ingest a compound, usually cocaine, wrapped in multiple condoms, in an attempt to smuggle the compound into a country such as the United States within their body. If one of the packages should rupture, the "packer" will be exposed to massive amounts of cocaine, probably with terminal results.
- Boost/boosting** This common process increases the CNS depressant effect of each class of drugs to induce or reinforce drug-induced euphoria at the risk of potentially lethal results.
- Borderline personality disorder** Disorder characterized by instability in relationships, sense of self, and emotions, that significantly impacts relationships with others on a long-term basis.
- Bromide salts** Introduced in the mid-1800s as a treatment for epilepsy, and then later as a sedative and hypnotic.
- Cannabidiol (CBD)** A compound inhaled when marijuana is smoked, that seems to have an inverse relationship with THC.
- Cannabinoids** Compounds that are manufactured and used in the brain to regulate neurotransmission, especially the *dopaminergic* neurons.
- Cardiomyopathy** Technically, any disease of the myocardium, the muscle tissue of the heart.
- Carisoprodol** An over-the-counter prodrug biotransformed in part into meprobamate after ingestion.
- Catecholamines** A family of compounds, including epinephrine, a compound normally produced by the adrenal glands, and the neurotransmitters norepinephrine and dopamine. These compounds help to regulate various body functions. Norepinephrine, for example, functions as a neurotransmitter in the brain.
- Ceiling dose effect** A dose above which additional drug molecules will not have any additional effect.
- Cerebellar ataxia** Loss of motor coordination and balance caused by damage to the cerebellum.
- Cerebellar atrophy** Shrinkage in the overall size of the cerebellum due to death of neurons in this region of the brain.
- Cerebellum** In terms of the total number of neurons, the cerebellum is the largest part of the brain, in spite of its relatively small size. It is involved in the process of coordinating motor activities in the body.
- Certified medical review officer (CMRO)** Physician who has been trained in the interpretation of urine toxicology test results. The CMRO is also responsible for the integrity of the urine toxicology testing procedures utilized for interpretation of unexpected test results, and is charged with maintenance of patient confidentiality in the testing process.
- Chippers** A subgroup of individuals who use a substance, who evidence a non-daily need to use that substance or who use it only occasionally.
- Chloral hydrate** A hypnotic prodrug originally marketed in 1870 for treatment of sleep issues.
- Choreoathetoid movement (crack dancing)** Bodily movements that are not controllable and are caused by cocaine use.
- Chronic stage** During this stage, the individual will demonstrate symptoms such as a deterioration in morals, the use of alcohol substitutes when ethyl alcohol is not available, or development of tremors after drinking.
- Cilia** Microscopic hairlike projections from the wall of various body organs, including the lungs, where they help to propel mucus to the top of the lungs, helping to expel foreign particles from the lungs.
- Cirrhosis** Condition during which individual liver cells die and are replaced by scar tissue.
- Cocaethylene** A toxic compound transformed from cocaine in the body in small amounts, thought to be 25–30 times as likely to induce death as cocaine.
- Codependency** A relational pattern characterized by enabling behaviors on an ongoing basis.
- Cognitive-behavioral therapy (CBT)** Therapy that helps the individual learn how to change cognitions and behaviors, in part by confronting irrational thoughts or beliefs.
- Coke paranoia** Symptoms of a psychosis that are very similar to symptoms seen in schizophrenia, caused by use of cocaine on a chronic basis.
- "Coke run"** Engaging in extended periods of continuous cocaine use, at times in an attempt to overpower cocaine-induced tolerance.
- Compulsive gambling** A disorder characterized by inability or difficulty controlling impulses to gamble.
- Conduct disorders** A childhood condition marked by behavioral dyscontrol, acting out behaviors, and sometimes poor academic achievement in a child of normal intelligence.
- Confabulation** A neurological disorder in which the individual is (a) unable to remember part of his/her past, and (b) will make up a history. Without collateral information, the individual's rendition of his/her past might actually seem plausible in many cases, making the need for collateral information imperative to detect such cases. Causes of confabulation include (but are not limited to) Korsakoff's syndrome. Thus, it is imperative that the assessor rule out other possible causes of confabulation before assuming that it is alcohol-related.
- Confounding variable** A variable in a research study that potentially can alter the outcome of the study. For example, not controlling for when a subject last ate is a confounding variable in a study of a new medicine's effects on blood sugar levels.
- Congeners** Flavoring agents mixed with liquors.
- Contemplation** Stage during which the individual begins to consider thoughts of stopping misuse of substances within the next six months.
- Contingency management** Process through which a person with a substance use disorder is trained to identify high-risk situations in advance, and then practices coping mechanisms to avoid relapsing.
- Co-occurring disorders** A term used to describe patients who suffer from one or more concurrent form of mental illness and one or more SUD.
- Corpus callosum** Region of the brain that transfers information from one hemisphere to the other.
- Corticogenesis** Production and maturation of new neurons in the cortex region of the brain.
- Cortisol** Enzyme normally found in the body, which is found at higher levels during times of stress. It is often referred to as a stress-fighting compound because of this.
- Crack cocaine** Cocaine prepared for smoking before sale.
- Crack lung** An asthma-like condition resulting from habitual use of crack, also known as chronic bronchitis.

Craving An intense, subjective, emotional, and physical experience of desire for a substance, that varies in intensity between individuals.

C-reactive protein Protein molecule involved in inflammatory response.

Creatinine Waste product of muscle activity, the level of which is usually constant. Laboratories have established cut-off levels above or below which the urine is assessed as being suspicious because of the abnormal creatinine levels.

Cross-reactivity False positive results in some toxicology tests, due to structural similarities between certain compounds.

Cross-tolerance Process through which an individual's tolerance to one compound, say alprazolam, is transferred to other compounds in the same class, such as diazepam, as well as to similar compounds such as ethyl alcohol (all of which, in the example provided, are CNS depressants).

Cyclooxygenase An enzyme involved in the process of prostaglandin production. One form of cyclooxygenase (COX-1) is involved in the regulation of kidney and stomach functions, where it carries out a protective function.

The second form of cyclooxygenase (COX-2) is produced by body tissues when damaged. About 60% of the chemical structures of COX-1 and COX-2 are the same. Unfortunately, the shared elements of the molecule are what is blocked by NSAIDs, which function as nonselective COX inhibitors. By blocking the action of both forms of cyclooxygenase, the NSAIDs interfere with the normal function of COX-1, when it is the effect of COX-2 that prompted the use of the NSAID. It is for this reason that patients with hypertension are advised not to use an NSAID unless directed to do so by a physician, or why a patient taking aspirin for inflammation might suffer gastrointestinal damage, for example.

Delirium tremens (DTs) A condition usually related to alcohol withdrawal, during which confusion and symptoms such as sweating, shaking, and irregular heart rate rapidly appear; can result in seizures and potentially death.

Δ FosB (delta FosB) A compound found in neurons that controls the process of manufacturing proteins within the neuron. Δ FosB is one of the *genetic transcription factors* which control when or if certain genes within the neuron become active. This compound is thought to be involved in the process of memory formation, although its exact role has not been delineated, and in the expression of resilience on the part of the person in the face of trauma or stress.

Δ -9-tetrahydro-cannabinol (THC) The chemical name for THC, the compound found to produce the majority of marijuana's effects.

Denial A defense mechanism that is a form of unconscious self-deception.

Detachment The process through which an individual who struggles with codependency learns to stop controlling the other person's life; the process by which the person determines and begins the process through which he or she will no longer support another individual's addiction.

Detection threshold The level of metabolites of a particular substance that must be present in order to show as positive in toxicology tests.

Detoxification Process of removing a toxin from the body; medical management of a person's withdrawal from alcohol/drugs.

Diagnostic inflation Unfortunate outcome of the process in which a poorly trained assessor or vague diagnostic criteria result in an ever-growing number of people being diagnosed with a condition that in reality they do not have. This results in unnecessary referrals for treatment and blocks access to the available treatment resources for those who do need rehabilitation.

Diaphoresis Perspiration, especially copious amounts.

Differentiation "The ability to be in emotional contact with others yet still autonomous in one's emotional functioning" (Maté, 2010, p. 237).

Dimorphism See: *sexual dimorphism*.

Diphenhydramine An antihistamine with a strong sedative side effect.

Discontinuation syndrome The manifestations of the body's reaction when a compound regularly used as prescribed is either discontinued or markedly reduced. This is essentially a *withdrawal syndrome* from that compound, a term that offended many patients who were taking the compound as prescribed. To differentiate between the process of withdrawal from a prescribed as opposed to an illicit substance, the term *discontinuation syndrome* is used with the person who is withdrawing from a prescribed medication.

Disinhibition effect Effect after one or two drinks, caused when alcohol interferes with the normal function of the cortex region responsible for inhibitions, as well as abstract thinking and speech.

Dissimulation A situation where the client provides false information in response to a question or test item.

Dissociative disorders A series of related conditions characterized by the individual detaching from reality for periods of time to escape extreme psychological stress.

Dissociative identity disorder The most extreme form of dissociative disorders, in which an individual manifests more than one distinct personality.

Distillation Boiling wine, then collecting and cooling the steam to form a liquid with a higher alcohol concentration than the original wine.

Doctor making See: *"making" doctors*.

Doctor shopping Slang term for going to a number of different physicians until the substance abuser finds one who agrees that they might have a given condition and is willing to prescribe a desired substance for the treatment of a nonexistent or exaggerated condition.

Dopamine Neurotransmitter utilized in the brain for such tasks as controlling behavior and mood, motivation reward, learning, as well as some psychomotor functions. It is also involved in the reward cascade.

Dopaminergic Nerve cells that use dopamine as their primary neurotransmitter.

Dose-response curve A graphic representation of the physiological response of the user's body to a given compound.

Down-regulation Process through which a neuron decreases the number of receptor sites in response to large amounts of the enzyme or neurotransmitter at the receptor site, making that neuron less sensitive to that enzyme or neurotransmitter.

Dysentery A painful infection of the lower intestinal tract, usually caused by the ingestion of contaminated water. The infected person will develop massive diarrhea, sometimes intermixed with blood and mucus. Unless the fluid loss caused by the diarrhea is rapidly controlled, dysentery can prove to be fatal after only a short period of time. Dysentery was common in the crowded, unsanitary military camps of the 1700s and 1800s, as well as in many cities throughout history, and major epidemics of dysentery were recorded before the cause of the disorder was identified.

Dysphoria Feelings of sadness, sorrow, depression, etc. The opposite of *euphoria*.

Dysthymia The analogy to the former construct of "depressive neurosis" is not entirely inappropriate here. Technically, the term "dysthymia" means "ill-humored." Patients with dysthymia demonstrate depressed mood that lasts most of the day, and is continuously present. The individual will struggle with feelings of low self-esteem, inadequacy, irritability, and anger. They withdraw from others, lose interest in hobbies, and report that they have always felt depressed.

- Unlike major depression, dysthymia begins early in life, often in childhood, and is most certainly present by young adulthood, although there is a subtype that does not manifest until middle age or even later in life. The symptoms must be present for at least 2 years prior to diagnosis, and the disorder has an intermittent course.
- Early-onset alcoholism** A pattern of problems with alcohol in young adulthood, which continues through middle adulthood into the late adult years.
- Eating disorders** Disorders characterized by severe disturbances in behaviors related to eating.
- Edema** Swelling of tissues immediately adjacent to injury.
- Edibles** Term used to refer to marijuana prepared in products for oral ingestion.
- Effective dose** Dose response calculations of the approximate dose at which a given percentage of the population will respond to a given dose of a compound.
- Ejection fraction** The percentage of blood ejected from the heart's left ventricle each time the heart beats. In healthy individuals this is usually around 60–65%.
- Elimination half-life** The time that the body requires to eliminate 50% of a compound.
- Enabler** Any person who acts to protect a person with an SUD from the full consequences of her or his behavior.
- Enabling** To knowingly behave in such a manner as to make it possible for another person to continue to misuse chemicals, or in a manner that protects the person misusing substances from having to suffer the natural consequences of his or her behavior.
- Endocannabinoid** One of a family of compounds bound within the brain or body where molecules of compounds found in marijuana bind. These natural, or endogenous, cannabis-like compounds carry out essential functions such as guiding the growth of neural cells in the cortex in utero and after birth, regulation of the immune system, etc.
- Enkephalins** One of the family of endogenous opioids involved in the process of regulating pain.
- Enmeshment** Extreme involvement in the life of another person, such that the person believes the family member with an SUD is somehow a reflection on himself or herself.
- Enteral** Entering the body by the gastrointestinal tract, usually by oral administration.
- Epigenesis** Process through which the environment impacts how cells in the body produce protein molecules. This is accomplished by having certain molecules attach themselves to the DNA sequence, preventing the expression of genes beyond that point. In other words, the environment has been found to alter the expression of cellular DNA. It has been suggested that these alterations in DNA might then be passed from one generation to the next.
- Epigenetics** The field of study that explores how environmental forces alter the expression of genes.
- Epileptogenic** A compound that lowers the seizure threshold, or which can induce seizures in a person.
- Epinephrine** Also called adrenaline. Major excitatory neurotransmitter, produced by the adrenal glands, which sit on top of the kidneys. It is produced and released when the individual requires a burst of energy (as in the fight-or-flight syndrome) and when the individual is under stress.
- Euphoric recall** Tendency on the part of a person to remember past experiences in a positive light, while overlooking negative experiences associated with the same event(s). For example, a heavy drinker might drive by a bar and turn to a companion and say, "Didn't we have a great time at the boss's birthday party?" only to have the companion remind them that they were also arrested for driving under the influence of alcohol on the way home, and had to both spend time in the county jail and pay a fine of over \$1,000. These latter consequences are overlooked in favor of the positive memories of the night in question.
- Executive functioning** Essentially the ability of the individual to plan ahead, anticipate the consequences of his or her actions, etc.
- Externalizing disorder** Cluster of psychiatric symptoms seen in the antisocial personality disorder in adults, conduct disorder in children, and/or attention deficit hyperactivity disorder (ADHD).
- Faith** The development and expression of confidence in the tools and goals of one's spiritual journey in the face of doubt.
- Family disease model** Model that postulates that substance misuse in the family unit is an illness of the entire family and not just of the person misusing substances.
- "Fast" metabolizer** An individual whose body is, as a result of normal genetic variation(s), able to biotransform a compound more rapidly than average. This phenomenon is independent of those cases where the person is taking one compound that induces the biotransformation or metabolism of another through enzyme induction, etc.
- Filler(s)** When drugs are prepared for oral administration, pharmaceutical companies will mix the active agent with compounds designed to give the pill or capsule shape and form. These compounds are designed to be destroyed by gastric juices (thus releasing the active compound for absorption), or to break down in the gastrointestinal tract and release the active agent so that it might be absorbed.
- Intravenous drug abusers who crush a pill or capsule bypass the defenses of the gastrointestinal tract, and run the risk that these fillers might cause a blockage in a vein or artery.
- First-order biotransformation** A set percentage of a compounds in question is biotransformed each hour, independent of the concentration of that substance in the blood.
- First-pass metabolism** Over time, the body has developed a safety mechanism in which materials absorbed through the gastrointestinal tract are first carried to the liver, so that toxic compounds ingested might be subjected to detoxification before they can injure the body.
- Fixed-dosing regimen** A medication regimen in which a specified amount of a medication is administered on a fixed schedule.
- fMRI** See: *functional magnetic resonance imaging*.
- Formication** The sensation of having unseen bugs crawling on or just under the skin. This sensation is often induced by large doses of some chemicals, such as the amphetamines or cocaine.
- Free-floating denial (or interchangeable denial)** When a client with co-occurring disorders uses problems induced by one disorder to protect the other disorder.
- Free radicals** Molecules that, because of their ionic charge, are able to attach to and damage other molecules, thus disrupting the normal function of cells and possibly contributing to cellular death. Free radical molecules often contain an extra oxygen molecule, which will then bind to molecules found in cell walls, causing damage to them.
- Functional magnetic resonance imaging (fMRI)** Modification of the *magnetic resonance imaging (MRI)* procedure designed to measure levels of energy released by hemoglobin molecules in the blood of a designated region of the body when the magnetic field utilized in the MRI process is switched off. This provides a measure of oxygenated blood being used by the identified tissues and thus is an indirect measure of the level of activity of that region of the body.
- GABA** See: *gamma-amino-butyric acid*.
- Galactorrhea** Production of excess amounts of milk by the breast.
- Gamma-amino-butyric acid** Also known as GABA. During the period of embryonic brain development, GABA serves a stimulatory

function, assisting in the development of neurons in the growing brain. Following birth, GABA's role changes until it becomes the brain's main inhibitory neurotransmitter. Approximately 20% of the receptor sites in the mature brain are thought to utilize GABA, including neurons in the *cortex*, *cerebellum*, the *amygdala*, and the *nucleus accumbens*.

It has been discovered that there are two main subtypes of GABA receptors in the brain: GABA_A and GABA_B. Scientists are mapping the distribution pattern and function of these subtypes to better understand GABA's function in the brain.

Gastritis Inflammation of the stomach lining.

Gene expression The strength with which the information encoded on a gene influences the biological function of the cells in the body.

Generalized anxiety disorder A disorder characterized by excessive worry, usually about numerous things.

Gestalt A German word that does not readily translatable into English. The concept that the whole is greater than the sum of its individual parts conveys part of the meaning of this word. "Unity of being" also conveys part of the meaning.

Glial cells There are a number of subtypes of glial cells in the brain, including Schwann cells, Muller cells, epithelial cells, oligodendrocytes, and astrocytes, to name a few. Collectively, the glial cells make up 90% of the cells in the brain. Yet for a long time they were dismissed as providing only structural and metabolic support for the neurons, which comprise 10% of the brain's mass.

Some glial cells have been found to "monitor" the neurotransmission process between neurons, and to modulate the process of neurotransmission at times. They have also been discovered to be capable of forms of intercellular communications that can utilize some of the same neurotransmitters as neurons, as well as distinctly separate forms of intercellular communications. Scientists are only now starting to understand that these cells are actively involved in the process of information processing, memory, and cellular repair following damage to the brain.

Glioma Cancer arising from the glial cells in the brain.

Glossitis A very painful inflammation of the tongue.

Glucocorticoids Class of steroids involved in the stress response process, metabolism of sugar in the body, suppression of the inflammatory response, and suppression of the immune system response.

Glutamate A major excitatory neurotransmitter that is found in much of the brain. It is also involved in the process of learning and memory. Preliminary evidence also suggests that glutamate might play a role in the development of schizophrenia and depression, as well as post-traumatic stress disorder. Excessive amounts of glutamate can prove to be neurotoxic, damaging or killing neurons in high doses.

Glutethimide A compound introduced in the 1950s as a replacement for barbiturates, with a chemical structure similar to barbiturates.

Grave's disease A dysfunction of the thyroid gland in which the thyroid produces too much thyroid hormone. This in turn interferes with the normal function of the thyroid.

"Gray" amnesia or "gray out" Condition in which individuals have some limited memories of events that transpired while they were intoxicated, intermixed with periods of total amnesia.

Gray matter The neurons in the cortex of the brain appear gray during an autopsy, hence the name. In the living brain they have a vivid, reddish brown color under normal conditions, a sight that is rarely seen except by neurosurgeons.

The cortex is the region of the brain where the so-called "higher functions" such as thought and planning take place. Some regions of the cortex are also responsible for planning and initiation of psychomotor activities, speech, and hearing.

Group therapy Generic term for a wide variety of therapeutic approaches carried out in a group setting.

Half-life (of a drug) The *rough* estimate of a compound's effectiveness, duration of effect, and the length of time that it will remain in the body.

Hashish Thick resin high in THC, obtained from the flowers of the cannabis plant.

Hash oil Liquid extract from the cannabis plant, usually containing 25–60% THC.

Hectare Unit of land measurement 100 meters × 100 meters square. This is an area about 2.471 acres in size.

Hemp The term used for cannabis plants grown for their ability to produce fiber.

Hepatotoxicity Toxic to the liver.

Hippocampus A region of the brain that is thought to be involved in processing sensory information, as well as the formation and retrieval of memories. In normal healthy adults, it appears to shrink by 0.5% per year, although the importance of this data to the additions is not clear at this time. The possibility exists that continuous exposure to alcohol or drugs of abuse might exacerbate this shrinkage and contribute to the development of depression seen in many alcohol/drug abusers, although this has not been proven.

H-P-A axis The hypothalamus and pituitary regions of the brain, plus the adrenal glands, are involved in the body's response to real (or perceived) threats, ultimately increasing the release of stress-fighting hormones such as cortisol in the body.

Huffing Pouring a compound onto a rag, which is then placed over the mouth and nose to inhale the fumes.

Hypertension Abnormally high blood pressure.

Hyperthermia Retention of body heat well above safe levels, which may prove fatal to the individual if not corrected before the brain is damaged by the abnormally high body temperature.

Hypnotic A compound that can induce sleep, or a sleep-like state.

Hypokalemia Abnormally low blood potassium levels.

Hypothalamus A region of the brain that controls behaviors such as eating, fighting, sleeping, and mating.

Hypothermia Abnormally low body temperature, which if not corrected in a timely manner might result in the individual's death.

Hypoxia Reduced oxygen flow to the brain. This can result in organic brain damage if not rapidly corrected.

Iatrogenic Literally, induced by a physician. This term is also often applied to conditions that are side effects of treatment of another disease, such as antibiotic-induced diarrhea where the antibiotic compound is used to treat a serious infection elsewhere in the body.

"Ice" A form of methamphetamine prepared for smoking, concentrated into a crystal that resembles a chip of ice or a piece of clear rock candy.

Illusion of correlation The tendency to remember events that confirm preconceptions and dismiss or forget information that fails to do so.

Individuation A term developed by Carl Jung for the process of becoming aware of one's inner "self," including expectations about how others behave and how the world functions. This process is influenced by social and cultural forces, but especially by the family environment in which the child is raised.

Individuals who suffer from failure to individuate from caregivers fail to develop their own feelings, thoughts, or independence, basing their reactions to new situations on their expectation of how the significant other(s) will react. During infancy and very early childhood this is natural, but in a healthy family the child will be encouraged to gradually learn to leave the protection of the family

- environment, learn their own emotional responses to life's experiences, make mistakes from which they learn valuable lessons, and become a self-aware, responsible adult who possesses the power of self-determination and the ego strength to accept the responsibility for their choices. See the works of Murray Bowen (far too numerous to list here) for a further explanation of this concept.
- Inhalant** Term used to describe the method of substance use that introduces any of a wide variety of compounds into the body by inhaling.
- Inhalation** Administration by inhaling a substance, usually in aerosol or similar form.
- Innate tolerance** Preexisting tolerance to the presence of narcotic (or other substance) molecules.
- Inpatient substance rehabilitation treatment** A treatment setting that provides a 24-hour treatment milieu, with staff members on duty 24 hours a day.
- Integrated treatment program** A treatment approach that focuses on treating the SUD and the psychiatric problems simultaneously, by a variety of professionals focusing on a team approach to help the individual.
- Intervention** An organized effort by a person or persons who are part of the environment of the individual with an SUD to break through the walls of denial and rationalizations that surround the addictive behaviors; often supervised by a trained professional, with the goal of obtaining an agreement from the person struggling with the SUD to immediately seek admission to a designated treatment center.
- Intramuscular** Injection of a compound in the muscle tissue.
- Intranasal** Administration where compound is "snorted," depositing it on to the blood-rich tissues on the sinuses.
- Intravenous** Injected directly into a vein.
- Isomer** One of two or more compounds with the same percentage of chemicals, but where the molecular structure of the chemical is slightly different.
- Kindling** A process that has been called "reverse tolerance" by some scientists. Through the process of kindling, the brain becomes more and more sensitive to seizure triggers, which then initiates a seizure(s). Sometimes this process is called *sensitization*.
- Lapse** When the individual initially uses a compound after a period of abstinence, such as the first puff of a marijuana cigarette or the first swallow of alcohol.
- Late-onset alcoholism** Those individuals who did not show evidence of an AUD in young or middle adulthood, but who did develop an AUD in late adulthood.
- Late-onset exacerbation** Older adults with AUDs who had intermittent problems with alcohol in young and middle adulthood, but did not develop a habitual pattern of alcohol misuse until late adulthood.
- Law of unintended consequences** A rule that whenever a change is made, it alters the system in unforeseen ways, resulting in stressors and complications that were not expected when the original change was made.
- An excellent example of this law is the application of high-cost, labor-intensive medical care to treat heart attack victims. This results in increased survival rates (the intended result), but also leaves a pool of heart attack survivors who require intensive medical monitoring afterward (unanticipated consequence), placing an unanticipated drain on the health care system.
- Lipid-soluble (lipophilic)** The characteristics of some drug molecules that allow them to bind to one of the fat molecules that circulate through the body.
- Liver** Vital organ in the human body located under the rib cage on the right-hand side. This organ carries out over 5,000 known functions, including biotransformation of medications, hormone balance, cholesterol breakdown, and metabolism of environmental toxins.
- Lymphocytes** Generalized disease-fighting cells.
- Machiavelli, Niccolo** (May 3, 1469–June 21, 1527). Italian historian and philosopher whose book *The Prince* has been accepted as an illustration of the philosophy that the ends justify the means for those in power to obtain their desires.
- Machiavellian** See *Machiavelli, Niccolo*.
- Macrophage cells** Generalist cells from the immune system that help to clean up cellular debris and attack foreign cells. Macrophages are also involved in some aspect(s) of the immune response.
- Magnetic resonance imaging (MRI)** An imaging procedure in which a strong magnetic field is generated, forcing atoms with odd atomic weights to align with the magnetic field. Then the field is switched off and the energy generated when these atoms swing back to their normal position is measured.
- Maintenance stage** Stage during which the individual develops behaviors supportive of recovery, addressing problem areas ignored during active substance misuse, and confronting personal issues that contributed to or exacerbated the SUD.
- "Making" doctors** A variation of *doctor shopping* in which the individual with a substance use disorder obtains a prescription under false pretenses. Sometimes this involves switching to a new health care provider and providing false information in the hope that the health care provider does not have access to the individual's prior medical records.
- Liebrez and colleagues (2015) gave an example of a person who went to see a new doctor and told that doctor that he had a prescription from his previous physician for 80 mg/day of diazepam, when in reality the original health care provider had prescribed only 20 mg/day. The individual now has an extra 60 mg/day to use as he/she might decide.
- Marijuana** Term used for cannabis plants grown for their ability to produce compounds with a psychoactive effect.
- Marital and family therapy** A generic term applied to a number of different therapeutic approaches including the psychodynamic, family systems, structural, and behavioral family therapy approaches.
- Mead** Form of beer made from fermented honey.
- Meconium** A thick, green, tar-like substance that lines the intestinal tract of the fetus. This substance is usually excreted by the infant in the first few days after birth. Occasionally it is excreted before or during birth. If it is excreted prior to birth, physicians may try to dilute it by injecting sterile fluid into the uterus to dilute any meconium in that environment. If aspirated by the neonate during the birth process, it is called *meconium aspiration syndrome*. This is a medical emergency. Following birth it can prevent the infant's lungs from properly inflating, and may cause pneumonia.
- Medulla oblongata** Region of the brain, sometimes referred to as the brain stem, involved in the control of respiration and temperature regulation.
- Melatonin** Hormone produced by the pineal gland in the brain, the actions of which in the brain are still not well understood. It is thought that this compound plays a role in the regulation of human circadian rhythms.
- Mellanby effect** A phenomenon in which the individual's subjective sense of intoxication appears to be stronger while the BAL is still rising.
- Meningioma** A tumor of the central nervous system that is usually classified as a *space-occupying lesion* rather than an invasive tumor.

There is some debate about whether it should be classified as a form of cancer. Typically, meningioma growth is slow and the brain is often able to compensate for the tumor's presence for years if not decades. The meningioma is frequently found as an incidental discovery, such as when a patient has a C-T scan to rule out a fractured skull following a motor vehicle accident.

Meningiomas can grow to an impressive size before producing symptoms that call attention to their presence. The symptoms produced by a meningioma depend on the specific location where it is located.

Mensch A person with fortitude ("guts") and/or firmness of purpose. Strength of character.

Meprobamate First introduced in 1955 as a "nonbarbiturate" compound that could be used in the daytime to treat anxiety and at higher dosage levels as a hypnotic agent, with a chemical structure similar to that of the barbiturates.

Messenger RNA A molecule that is formed within the cell nucleus by copying half of the DNA molecule and then carrying these genetic instructions through the nucleus wall to the cell. This then "programs" the cell to follow the instructions on the messenger RNA molecule.

Methaqualone Often known as quaaludes, introduced as a safe, "nonaddicting" barbiturate substitute in 1965.

Methyl alcohol Also known as *wood grain alcohol*, or *methanol*, this is one of the alcohol family of compounds. It is very toxic to the human body, with the estimated lethal dose being just two teaspoons for a child and a quarter of a cup for an adult.

During the Prohibition era, methyl alcohol was often mixed with industrial alcohol solvents to discourage the diversion of these chemicals to the illegal alcohol trade. The government ordered this on the theory that if the drinker knew of the dangers associated with drinking methyl alcohol he or she would not consume drinks made from diverted industrial solvents.

This theory was not supported by fact, and resulted in thousands of needless deaths in persons who were unaware of the presence of methyl alcohol in their drink. The same enzymes that break down ethyl alcohol so easily struggle to biotransform methyl alcohol, producing formaldehyde and formic acid as intermediate metabolites. These compounds in turn destroy the retina, optic nerve, parietal cortex of the brain, and the lungs. Respiratory failure is the usual cause of death, although if the individual should survive there is the chance of permanent blindness.

Microcephaly A condition in which a baby's head is below the 5th percentile for infant head circumference.

Minimization A defense mechanism with which an individual consciously or unconsciously reduces the impact of a socially unacceptable behavior or its effects on others.

Miosis Constriction of the pupils of the eyes.

Mnemonic Something that aids memory. A mnemonic device might be a series of letters that remind a person such as a health care professional to address certain issues. For example, the letters "A-B-C" remind the health care professional to check the patient's *airway*, *breathing*, and *circulation*, immediately.

"Molly" A popular street name often applied to crystalized MDMA.

Monoamine oxidase Enzyme produced by the brain to break down members of the neurotransmitter family known as *monoamines*.

Monoamine oxidase inhibitor (MAO inhibitor, or MAOI) Any of a number of compounds that will block the actions of the enzyme monoamine oxidase.

Motivational interviewing A therapeutic technique used in short-term intervention therapy that places great emphasis on helping the

individual identify how one is currently living and how one wishes to be living in the future.

mRNA Also known as *messenger RNA*. A form of ribonucleic acid that carries directions from the DNA in the cell nucleus to the interior of the cell.

Myocardial infarction The blockage of blood to the tissue of the myocardium, which is to say the tissues of the heart. If this blood flow is not restored in a short period of time, the tissue will die. Often called a "heart attack" by the layperson.

Myocardial infarction gender gap Nonsmoking women tend to experience heart attacks 10 years later than men.

Narcolepsy Neurological condition in which the patient will experience sudden attacks of sleep.

Necrosis Death of body tissues.

Neuroadaptation The process, once called "tolerance," by which the nervous system adapts to the constant presence of a foreign compound. This usually involves modification of the receptor sites on the neurons affected by that compound. This term is usually applied to the brain's adjustments to the constant presence of a prescribed chemical, while the term "tolerance" is applied to the same process when it involves an illicit compound.

Neurogenesis Growth of new neurons.

Neuroplasticity Ability of neurons to form new neural pathways in response to new experiences (what we call learning), and, to some degree, after neurological trauma.

Neurotoxin A chemical that is toxic to the neurons in the brain.

Neurotransmitter Any molecule that is released by one neuron to pass a chemical-electrical message on to the next neuron. This then causes the target neuron to respond to the chemical message passed on by the first neuron in a specific manner.

NMDA See: *N-methyl-D-aspartate*.

N-methyl-D-aspartate Protein that forms a receptor site in the neural wall for the excitatory neurotransmitter glutamate.

Norepinephrine One of the catecholamine family of neurotransmitters. In the central nervous system, norepinephrine serves a stimulatory function.

Nucleus accumbens Region of the brain thought to be responsible for reward and motivation. At one point, the nucleus accumbens was thought to be the reward center in the brain. It has now been discovered that environmental stimuli (both reinforcing and aversive) stimulate a release of dopamine from the nucleus accumbens, suggesting that it signals that there is a change in the external environment that requires attention.

It is known that this region of the brain is involved in the process of integrating the individual's conscious activities with sensory stimuli. It is most active when the body encounters an *unexpected* event, either positive or negative. When a reward becomes anticipated, other regions of the brain seem to become involved in the reward cascade and the nucleus accumbens becomes less active.

Obsessive compulsive disorder A disorder characterized by significant obsessions and compulsions that significantly impact daily life.

Obstructive sleep apnea Condition in which the airway becomes blocked during sleep for longer than 10 seconds. The sleeping person must then struggle to reopen the airway, often through gasping, snorting, or coughing. This is a medical problem that should be addressed by a physician if it is suspected to exist.

Occult insomnia Sleep disturbance occurring when cocaine use is discontinued, where individual may be sleeping less than they realize.

"Off-label" application The application of a pharmaceutical for a disease or condition that it is not normally licensed for. The Food

- and Drug Administration often will not approve an existing medication for a new use it has not conducted or supervised testing on the efficacy and safety of that compound in that application, a process that might take months, or even years. During that time, physicians will often use the compound to treat a disease(s) or condition(s) based on research data from Europe, or anecdotal data.
- Oppositional defiant disorder** A behavioral disorder in which a child demonstrates temper outbursts, actively refuses to comply with rules, and engages in annoying behaviors far in excess of what one would expect from the child on the basis of chronological age. There is an enduring pattern of negativistic, hostile, and defiant behaviors involving violations of social norms or the rights of others.
- Outpatient substance rehabilitation program** A formal treatment program involving one or more rehabilitation professionals, designed to help the person with an SUD develop and maintain a recovery program which will utilize a variety of treatment approaches on an outpatient basis.
- Over-pressure** Above the ambient atmospheric pressure. In the case of surgical anesthetics, pure oxygen must be supplied to the patient at over-pressure, to avoid the danger of *hypoxia*.
- Over-the-counter (medication)** There are more than 100,000 compounds that may be purchased without a prescription, thus earning the title of an over-the-counter compound.
- Oxytocin** Functions both as a hormone and neurotransmitter. It is involved in such functions as labor, production of breast milk, maternal love, romantic love, and the development of trust.
- Paraldehyde** A hypnotic that produces a noxious taste and unpleasant breath, first introduced as a hypnotic in 1882.
- Parallel treatment model** A treatment approach that focuses on treating the issues simultaneously, in different sections of the facility, but without a team approach.
- Parasympathetic nervous system** Portion of the central nervous system involved in helping to regulate the body's unconscious activities such as blood pressure control, etc. The parasympathetic nervous system counters stimulatory effects of the sympathetic nervous system, which controls activities such as the fight-or-flight response. Thus, the parasympathetic nervous system helps the body to rest so that the individual can focus attention on eating and social relationships (including sexual arousal).
- Parenteral** Entering the body by injection.
- Pericytes** Cells in the brain that help to stabilize the blood-brain barrier.
- Peristalsis** Rhythmic contractions of the muscles that surround the intestines, pushing the ingested material through.
- Personality disorders** Disorders characterized by inflexible patterns that significantly impact relationships with others on a long-term basis.
- PET scan** Abbreviation for positron emission tomography. This process produces three-dimensional images of specific organs after a molecule "tagged" with a radioactive substance is injected. Special detectors measure the regions that have absorbed the most of the compound (usually glucose), allowing a computer to build a 3-D image of that region of the body.
- Pharmaceuticals** (1) Compounds produced under supervision of various regulatory agencies, intended for the treatment of disease states in humans or (if veterinary medications) animals. Such compounds are of a known potency and purity.
(2) Term applied to compounds intended for medical use that are diverted to the illicit drug market. As such, they are often prized by drug abusers, since they are known to be pure, and not adulterated as illicit drugs often are.
- Pharmacodynamics** The way in which a drug impacts the body, including for how long and how strong.
- Pharmacokinetics** How time impacts a drug moving through the body.
- Photosensitivity** An extreme sensitivity to sunlight, which can be caused by some medications.
- Phrenology** A pseudo-science popular in the 1890s that asserted that you could deduce a person's character on the basis of the bumps in the skull. Proponents of this belief developed numerous maps and models of the skull, attributing various personality characteristics to these normal variations in skull structure.
- Physical dependence** Evidenced by the experience of the characteristic alcohol withdrawal syndrome when an individual suddenly stops drinking.
- Pituitary gland** Structure in the brain that has been called the "master gland" in the body. It activates a number of other glands through the release of hormones through the blood, thus controlling growth, to cite one example.
- Placebo effect** A phenomenon that illustrates how much power expectations have over the actual effects of a chemical(s). We *expect* that a drug or medication will have a certain effect on us and interpret subsequent side effects or even incidental bodily actions as evidence that the chemical is having its intended effect and causing us to experience the effects that we expect.
Some researchers in the field have suggested that for certain classes of medications, the user's expectations might account for as much as 40% of the reported effectiveness.
- Pneumonia** Acute infection of the lungs, usually caused by bacteria or fungi.
- Pneumothorax** A condition during which the alveoli of the lungs rupture, allowing air and bacteria to escape into surrounding tissues.
- Polypharmacology** Concurrent use of multiple agents. This may take place both in therapeutic settings and in the world of illicit drug use. One danger of this practice is the *potentiation* or *synergistic* effect between compounds in the same class of chemicals.
- Polyphenols** Family of natural, semisynthetic, and synthetic compounds that have chemical similarities (essentially the phenol structures in the molecule). Some of these compounds are useful for humans, while others are harmful, depending on the exact chemical structure of the specific polyphenol molecule. Some of the nontoxic polyphenols are found in wine, helping to give the wine a specific flavor.
- Positron emission tomography** See: *PET scan*.
- Potentiation** The pharmacological process through which the effects of one compound are reinforced by those of a second compound. This may prove to be fatal for the individual if the combined effects of the chemicals overwhelm the body's normal maintenance mechanisms.
- Precontemplation** Stage during which the individual misusing substances has no thought of trying to abstain from the misuse within the next six months.
- Prefrontal cortex** Region of the brain that, among other things, is involved in complex cognitive and psychomotor processes including self-regulation of goal-directed behavior, working memory, problem solving, and response inhibition.
- Preparation** Stage during which the individual misusing substances is ready to change attitudes and behaviors, and may have begun the initial steps of the change process.
- Presynaptic** Involving the "upstream" neuron, which is to say the neuron that releases neurotransmitters into the synaptic junction to activate the next neuron in the neural network.
- Presystemic elimination** The effect by which the human digestive tract is designed not to let any chemical that is absorbed pass directly into circulation, but to filter it first through the liver.

Priapism Extended, painful penile erection, which may cause damage to the vasculature network of the penis and possibly result in permanent erectile dysfunction.

Prime effect (of a drug) The desired effect of the compound. For example, a person who has a fever might take an aspirin tablet with the goal of reducing his/her fever to a more tolerable level. Compare this with the *side effect* of a compound. This is sometimes referred to as the *therapeutic effect* of the compound.

Prodromal stage During this stage the individual begins to demonstrate alcohol-related problems, such as blackouts, guilt over their behavior while intoxicated, and the urge to hide their drinking from others.

Prodrug (pro-drug) Compound that must be biotransformed into another compound to have the desired effect.

Projection A defense mechanism in which material that is not acceptable to oneself is projected onto others instead.

Prostaglandin(s) Any of a family of compounds found in the body, some of which are involved in normal maintenance of body organs and some of which are involved in the inflammatory response following injury. These compounds are active in very low concentrations.

Proteinuria Presence of abnormal levels of protein in urine, which may indicate kidney damage or disease.

Psychological dependence When an individual depends on alcohol (or another substance) for psychological support as well as a means to enhance the ability to cope with the demands of living.

Pulmonary arteritis See: *arteritis*.

"Pusher" One who sells illicit drugs.

Rapid metabolizer Individual who is able to biotransform a given compound more rapidly than is typical of the average person.

Rationalization A defense mechanism used to justify otherwise unacceptable behaviors through cognitive justifications.

Rebound insomnia A phenomenon resulting from discontinuation of benzodiazepines, forcing the individual to endure episodes of insomnia until the body adapts to the absence of the substances.

Relapse When a person falls back into active disease state after a period of remission.

Relapse prevention A self-management program designed to assist the individual in arresting his or her SUD to the best degree possible.

Religion An organized set of beliefs, which are often described in the texts considered sacred by followers of the particular religion.

REM "rebound" Increase in the duration and frequency of the REM sleep stage, often with intense, vivid imagery that might border on nightmares. This is thought to reflect the brain's attempt to "catch up" on lost REM sleep time from sleep deprivation or drug-induced suppression of this stage of the sleep cycle.

Reperfusion Sudden restoration of blood flow to a region of the body that had been deprived of blood. The damage caused by the actual cessation of blood flow to that region of the body might be exacerbated by the sudden restoration of circulation to the affected cells.

Reticular activating system (RAS) A small region of the brain, possibly only 100 neurons in size, which is responsible for the individual's ability to focus attention on the task at hand.

As scientists have learned to identify the primary neurotransmitter(s) utilized by individual neurons, this term is increasingly falling into disfavor. Not surprisingly, excitatory neurotransmitters such as dopamine and acetylcholine are the primary neurotransmitters used by neurons in this region of the brain stem. These neurons are interconnected with substructures of the brain that help govern wakefulness and concentration.

Retrograde amnesia Inability of the individual to remember events prior to a specific time. This condition usually is the result of any of a number of forms of neurological trauma. It is not uncommon, for example, for patients to report that they were unable to remember having been in a motor vehicle accident, or that they only have incomplete memories of the accident and what happened in the moments before the accident.

Each patient must be assessed individually to determine the degree to which his/her memory capacity has been affected. It should be pointed out that anterograde and retrograde amnesia are not mutually exclusive, and may coexist in the same patient.

Reuptake pump Molecular structure located in the walls of a neuron that absorb molecules of a specific neurotransmitter after its release into the synapse for recycling by the neuron.

Reverse tolerance Poorly understood phenomenon in which lower doses of a compound produce the same effect as higher doses did when the use of the substance was initiated; also known as *sensitization*. When drinking alcohol on a chronic basis, an individual may not require as much alcohol to achieve a given level of intoxication as previously needed.

Rhabdomyolysis Destruction of muscle tissue on a massive scale. When muscle tissues die, they release a compound known as myoglobin, which normally helps to store oxygen in the muscle cell. During rhabdomyolysis, massive amounts of myoglobin are released into the circulation at once, which interferes with normal kidney function. In extreme cases, this can cause kidney failure, cardiac arrhythmias, and even death.

Rig Slang term for device used for intravenous drug injection.

Ritual A uniform time and procedure in each day's schedule.

Schizophrenia A disorder that is often characterized by difficulty understanding what is imagined from reality, speech or behavior that may be unusual, often showing withdrawn behaviors, and difficulties with typical daily activities.

Screening Process used to identify those patients who might have a certain disease or condition.

Secondary effect (of a drug) Unwanted side effects.

Selective androgen receptor modulators Class of compounds first introduced in 1999 that are nonsteroidal selective agonists mainly for the androgenic receptor sites in the body. This class of medications does tend to lack the cardiovascular side effects of anabolic steroids, making them of particular interest to those who use performance-enhancing compounds.

Self-selection bias Individuals who are in a given group self-select to be there, and thus are more likely to be ready for change.

Sensitization effect Almost a form of reverse tolerance, in which the brain becomes hypersensitive to the effects of, or presence of, a compound (such as cocaine), causing effects such as seizures or even death from doses once easily tolerated without ill effect. The concept of an allergy might not be entirely inappropriate here.

Serial treatment approach A treatment approach that focuses on treating the most serious issue until that condition is stabilized, and then the client is transferred so that other disorders might be addressed.

Serotonergic Pertaining to or using serotonin.

Serotonin One of the major neurotransmitters found in the human brain. There are 19 known subtypes of serotonin, each of which is thought to control different functions in the brain. As a group, these subforms are involved in regulation of body temperature, memory, sleep, mood, and appetite.

Serotonin syndrome A potentially life-threatening drug-induced neurological condition. In spite of the best medical care, up to 11%

of patients who develop this condition will fail to survive. Behavioral symptoms of the serotonin syndrome include irritability, confusion, increased anxiety, drowsiness, *hyperthermia*, *sinus tachycardia*, dilation of the pupils, nausea, muscle rigidity, and seizures.

The serotonin syndrome might develop up to 24 hours after a patient starts taking a medication that affects *serotonin*. In 50% of cases, the patient begins to develop the disorder within 2 hours of when s/he starts to take the medication.

All suspected cases of serotonin syndrome should be assessed by a physician immediately, as this condition can potentially be fatal. There is no specific treatment for serotonin syndrome, and the only treatment is supportive care (Boyer, 2005).

Sexual dimorphism Subtle differences between male and female.

Side effect (of a drug) The unintended effects of a chemical on the body. For example, if a person were to take a dose of aspirin to reduce his/her fever, this is the primary effect. The ability of aspirin to also induce gastrointestinal bleeding is an undesired, or side, effect of that compound.

Site of action Where a compound carries out its main effects.

Skin popping Term used by some individuals to refer to the subcutaneous method of drug administration, which is injecting the compound under the skin.

Sleep apnea A breathing disorder in which the individual's ability to breathe normally during sleep is disrupted. Complications of sleep apnea can include hypertension, heart rhythm disturbance, and possible death.

Sleep latency The period of time between when a person goes to bed and when s/he finally falls asleep.

Slow metabolizer As a result of normal genetic variation(s), there are individuals whose body biotransforms or metabolizes a compound more slowly than the average person. This phenomenon is independent of those cases where the person is taking one compound that blocks the biotransformation or metabolism of another.

Sniffing/snorting When a compound is inhaled directly from its container.

Social anxiety disorder A disorder characterized by significant struggles with everyday social situations.

Specific phobia A disorder characterized by excessive fear of a specific thing or situation.

Speedballing Term used to refer to the practice of using cocaine and a narcotic analgesic simultaneously.

"Speed run" When an individual injects more amphetamine every few minutes because of tolerance to the effects of the substance being misused.

Statistically significant A statistical determination that indicates the results of a research study were not due to chance.

Stimulant A term associated with many substances, including cocaine, that stimulate the individual in some way.

Stroke Interruption of blood flow to a region of the brain. In *ischemic* strokes, a blockage in a blood vessel forms, cutting off the neurons that rely on that vessel from the cerebral vasculature. Unless these neurons are able to draw on other blood vessels (collateral circulation), they will die. Statistically, 85% of strokes are ischemic strokes.

In a *hemorrhagic* stroke, a blood vessel in the cerebral vasculature ruptures. To prevent uncontrolled hemorrhage, the body then forms a blood clot in the damaged vessel, cutting off those neurons that depend on that vessel for access to the circulation from oxygen and nutrients. In addition, free blood is very toxic to the neurons, so the blood that flows from the ruptured vessel causes additional damage to the brain. Statistically, about 15% of strokes are hemorrhagic strokes.

Subcutaneous Injection of the compound just under the skin, allowing for a reservoir of the drug to be established in the body and a slower rate of absorption than the intravenous method.

Sublingual Administration under the tongue for absorption.

Symptom-triggered regimen A medication regimen that allows for medication dosage to be adjusted depending on the patient's symptoms.

Synapses (synaptic junction) Microscopic spaces that separate neurons.

Synergistic response A process through which two or more drugs of the same or similar mechanism of action reinforce the effects of each other, causing a stronger than normal response to each compound. The synergistic effect can potentially be fatal. Often called *potentiation* between the two compounds.

Synesthesia A phenomenon in which information from one sensory modality slips over into another sensory interpretation system. Persons who possess this ability naturally will speak of how they are able to see colors in association with certain sounds, for example. This phenomenon, which can occur naturally in rare cases, can also be induced by some drugs of abuse.

Taper A program in which gradually decreasing doses of a given compound are administered to a patient so that she or he might safely be taken off that compound.

Tardive dyskinesia Condition resulting in abnormal movements of muscles. Technically, the term "tardive" means "late," and dyskinesia refers to abnormal muscle movements. This condition was often seen as a late complication of Parkinson's disease.

However, certain compounds have been found to exacerbate the development of this condition. The abnormal muscle movements previously seen only as a late complication of Parkinson's disease are now seen in younger persons as a side effect of either medications or some drugs of abuse.

Telescoping A term applied to the accelerated progression from substance use through abuse to addiction.

Teratogen A compound that permanently interferes with normal fetal growth and development.

Teratogenic Harmful to the fetus.

Termination stage Stage during which an individual faces no temptations to use substances once misused.

THC The compound found to produce the majority of marijuana's effects, with the chemical name Δ -9-tetrahydro-cannabinol.

Therapeutic threshold The amount of a compound in the individual's circulation will increase until it reaches the minimal level at which that compound might be effective.

Therapeutic window (or index) The difference between the minimal effective dose of a medication and the level that will induce toxic effects. Alcohol, for example, has a "therapeutic" window of 1:3, which is to say that the amount of alcohol necessary to be ingested for its intended effect is about one-third of the amount necessary to induce toxic effects and possible death.

Thiamine One of the B family of vitamins. The B vitamins are thought to be involved in the maintenance of the nervous system. These vitamins are water-soluble, allowing the body to absorb the amount that it needs and then excrete the rest in the urine.

Thrombosis A blood clot that has broken off from a larger clot and is blocking a blood vessel, thus starving the tissue that relies on that vessel for oxygen and nutrients.

Tinnitus Loss of hearing, and a persistent "ringing" in the ears, which can be induced by loud noises, illness, or certain medications. This will gradually clear if the offending medications are discontinued immediately, but may become permanent.

Tolerance “A shortened duration and decreased intensity of drug effects after repeated administration” (Ghoneim, 2004b, p. 1279).

Torsade de pointes Cardiac arrhythmia that is potentially fatal.

Tourette’s syndrome A movement disorder in which the person will engage in repetitive, stereotypical movements, and often engage in repetitive vocalizations.

Transdermal Administration route for a compound to be slowly absorbed through the skin.

Transitional adolescent A person who is legally defined as an adult and who presents personality traits normally seen in young adults, as well as other traits more traditionally seen in adolescents.

Trans-species jump A process through which an infectious microbe will “jump” from its host species to another species. Glasser (2004) stated that of the more than 1,400 microorganisms that can infect humans, approximately half originally caused infections in animals and subsequently jumped to the human population.

The AIDS virus (HIV-1) is one virus that made such a trans-species jump, moving from chimpanzees to humans in the 1950s or perhaps earlier. Another such virus is the one that causes measles. Measles killed 8 million people around the world in 1974, before the start of immunization programs. By the year 2007 this figure had dropped to approximately 300,000 measles-induced deaths around the globe (Oldstone, 2010).

Unfortunately, people are becoming complacent about immunization against measles in the United States, where the virus once infected 500,000 people annually and killed about 500 of those infected. Lack of vaccination leaves children and uninfected individuals vulnerable to new waves of measles infection, as evidenced by sporadic regional outbreaks of the disease.

Traumatic brain injury (TBI) A nebulous term often used synonymously with the terms *head trauma* or *head injury*; identifies all possible injuries to the brain that may be found in the person who has experienced injury to the brain.

Tuberculosis (TB) An infection caused by one of the genetically similar strains of *Mycobacterium tuberculosis*.

Up-regulation Process through which a neuron increases the number of receptor sites in response to reduced amounts of a neurotransmitter or enzyme being present at the receptor site. This serves to increase the sensitivity of that neuron to the neurotransmitter or enzyme.

Vagus nerve Also referred to as the tenth cranial nerve, this nerve is actually comprised of a pair of nerves. The vagus nerve complex shares control of the cardiac rhythm through the *parasympathetic nervous system*, and thus is indirectly involved in dietary regulation, social relationships, and social relationships.

Vaping Term used for the vaporization of substances, such as marijuana.

Vasoconstriction Constriction of blood vessels, especially veins. This condition can develop in the brain, the vessels around the heart, or the peripheral regions of the body.

Ventral striatum Region of the brain involved in the integration of signals from the amygdala (emotional responses) with regions of the brain such as the hippocampus (memory functions) and cognitive/executive functions carried out by the prefrontal cortex regions of the brain.

Ventricular tachycardia Cardiac arrhythmia in which the normal pattern of electrical discharge and repolarization in the ventricles of the heart is interrupted, disrupting the normal heart rhythm. This condition is potentially fatal if not immediately corrected.

Vertical transmission Passing a virus from mother to infant, either during gestation or through giving birth.

Voucher-based treatment This form of treatment utilizes the distribution of vouchers for periods of confirmed abstinence.

Water-soluble Chemicals that are able to mix freely with the blood plasma.

White matter A region of the brain comprised of nerve cells responsible for the relay of information. The cortex is often referred to as “gray matter” after its appearance after death. In contrast to this, the other neurons in different regions of the brain assume a white color following death.

Abnormalities in the white matter of the brain will make it difficult for the individual to consider multiple viewpoints when making decisions, and in adolescents will result in the “one-track mind” so often seen during this phase of life.

Zero-order biotransformation The biotransformation mechanisms quickly become saturated, and only a set amount of a given compound can be biotransformed each hour, regardless of the concentration of the chemical in the brain.

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